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EPILEPSY: A PAROXYSMAL CEREBRAL DYSRHYTHMIA.[1]

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DISEASES change their names with increase, not of age (like Chinese children), but with increase of medical knowledge. Most disorders begin life bearing the name of the man who first recognized them or else they are temporarily tagged with some purely descriptive term. When the ætiology or pathology is discovered, the nomenclature is changed. Thus, *consumption* has become *tuberculosis*; *locomotor ataxia* has become *tabes dorsalis*; and *palpitation of the heart* has been classified into various disorders of cardiac rhythm as *paroxysmal tachycardia, auricular fibrillation*, &c.

However, some diseases never have outgrown their baby names. For example, ever since the days of Hippocrates, recurring and sudden loss of consciousness and of muscle control has been called "the falling sickness" or (in Greek) a seizure, "epilepsy." Thanks to the pioneer work of Berger in developing the electro-encephalograph, we can now make good the lack of thousands of years and adopt for this condition a name based on the underlying pathological physiology. We now know that epilepsy is due to the development of abnormal rhythms in the cerebral cortex; it is a *paroxysmal cerebral dysrhythmia.* This discovery places the study and understanding of epilepsy on a different and deeper level and requires a reorientation of our thinking.

We say "*a* dysrhythmia," because epilepsy is only one of many. For example, periodic breathing called "Cheyne-Stokes" respiration,

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is but the muscular registration of a medullary rhythm which is alternately slow and fast. Heart, viscera, endocrine glands, all have rhythms normal and abnormal.

We have presented elsewhere details of observations [1, 2, 3, 4] and certain interpretations of results [5, 6]. At this time we shall review in brief outline seven new facts about epilepsy which we have gained in the last two and a half years by means of electro-encephalography. In this period we have made records of about 400 epileptic patients, examining many of them repeatedly. Of these patients, 120 had from one to hundreds of seizures while connected with the apparatus. With the exception of the pioneer observations of Berger, who published records of abnormal rhythm which occurred during seizures (fact one of our list), we believe the observations which we have presented, or now present, are new.

(1) *A seizure is accompanied by disturbance in the normal electrical activity of the brain.*—More exactly, a clinically observed seizure is but the outward manifestation of a disordered rhythm of brain potentials. We have many hundreds of records made during clinical *petit mal*, and dozens made during *grand mal* or psychic equivalents. In every instance the abnormal rhythm was unmistakable. However, several of the 120 patients who had seizures under observation showed no abnormality of rhythm during the seizure. We believe that in these instances the disordered rhythm involved a portion of the brain other than that from which we were recording. We have seen tremendous electrical disturbances in one area unaccompanied by disturbances in surrounding areas. We can record the activity of as many as six cortical areas simultaneously so that we probably do not miss abnormal cortical rhythms when these involve the outer surface of the frontal, parietal or occipital lobes. All parts of the cortex are not accessible from the surface of the head, however, and more important, disturbances confined to subcortical areas would not be recorded. Those few seizures which were not accompanied by abnormal cortical rhythms were bizarre in their patterns, falling in the group of "epileptic variants." For example, in one child the seizure consisted of gagging, profuse salivation, and slight muscular rigidity with only partial loss of consciousness, symptoms suggesting subcortical origin. In certain cases of hyperactive carotid sinus reflex, no obvious abnormalities appeared in the electro-encephalograph when the patient lost consciousness after pressure had been applied to the carotid sinus. We may conclude that in all but 2 or 3 per cent. of epileptic patients, electrodes applied to the

scalp transmit characteristic and unmistakable evidence of an epileptic seizure.

If a patient has a tonic-clonic convulsion during which he shows no abnormalities of cortical activity, he can be put down as either hysterical or a malingerer, for the disturbance in *grand mal* involves the entire cortex and is therefore readily detected with electrodes on any part of

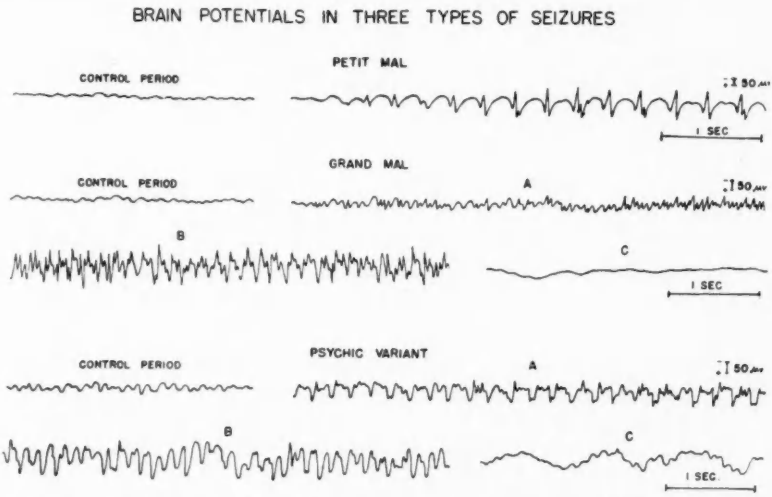

FIG. 1.—The wave formations which are characteristic of three types of epileptic seizures; *petit mal*, *grand mal*, and psychic variant. In each case the tracing under "control periods" was made in the normal period, before the seizure began. At the right is the signal made by 50 microvolts, and the space occupied by one second.

Petit mal.—The strip is the beginning of a *petit mal* record which lasted ten to fifteen seconds and then abruptly resumed the normal formation shown in the control period. The disturbance tends to have a slightly faster rhythm and smaller amplitude at the beginning. Between the start and the height of the seizure the rhythm may slow from 4 to 5 a second to 2 a second, and the voltage may increase from 50 to 500 microvolts. The *petit mal* formation is made up of two components, a wave with a duration of approximately one-third of a second, and a spike with a duration of one-tenth to one-twentieth of a second.

Grand mal.—The strip labelled A was made at the very onset of a *grand mal* seizure before clinical manifestations were present. There is an increase in the voltage of fast waves, those with frequencies around 20 per second. The strip marked B was made during the clonic phase of the fit. The fast waves are still present and still have an abnormally increased voltage, but they are now superimposed on slower waves which tend to be synchronous with the clonic jerks. The strip marked C was made during the post seizure stupor; all fast waves have disappeared and activity is confined to the frequencies of 2 to 3 a second. Voltage may be higher than in this record. As the patient regains consciousness, the normal rhythm gradually returns.

Psychic variant.—The strip labelled A was made at the beginning of the seizure. The patient stared, did not respond to questions, and when approached pushed the observer from him. The record is made up of square topped 4 per second waves on which are superimposed smaller waves of a faster rhythm and a higher voltage than seen in the control period. Strip B was made later when the patient was talking volubly but incoherently. It shows almost nothing but high voltage, square or round topped 6 to 7 per second waves. During the taking of strip C the patient was quiet but still mentally confused. This portion of the record resembled that seen in alcoholic intoxication.

the head. The absence of electrical abnormalities does not permit a differential diagnosis between hysteria and certain bizarre forms of epilepsy. The presence of abnormalities of the electro-encephalogram may, however, demonstrate that certain cases of unexplained muscle jerkings, temper tantrums, or moments of abstraction are really minute *petit mal* or psychomotor seizures.

(2) *The three types of seizures have distinct cerebral rhythms.*—With the patient connected to the electro-encephalograph, the operator in another room can tell not only that the patient is having a seizure, but also the sort of seizure he is experiencing. The pattern traced by the electro-encephalograph can be clearly classified into three main groups which agree with the three main clinical types of seizures (fig. 1). In all types there is during the height of the seizure a great increase in voltage. The point which distinguishes the three is the difference in the frequency of the waves. The normal frequency of the brain potentials is around 8 to 20 a second. In *grand mal* these waves speed up to 25 to 30 a second, and appear in our records as sharp spikes. In psychomotor attacks (psychic variants) the rate slows to 3 or 4 a second with a square, flat-top wave predominant. In *petit mal* quick sharp spikes and slow, round waves at the rate of 3 a second alternate. We can say explicitly that in *grand mal* the cortical activity is abnormally fast; in a psychomotor attack, it is abnormally slow; and in *petit mal*, it alternates between fast and slow. The exact pattern of the seizure record tends to be individual for each patient and tends to repeat itself in successive seizures.

(3) *Regulation of cortical rate.*—The abnormal rhythms which we have described are clearly the cause of those symptoms (loss of consciousness and abnormal muscle movements) which constitute the seizures of epilepsy. Yet the more fundamental basis of the disorder is not the abnormal rhythm, but rather a defective control of rhythm.

Each cell may be considered as a rhythmically acting unit, like a muscle cell in the heart, which contains electro-chemical mechanisms which regulate the frequency and amplitude of the cardiac contractions. When cells become organized into tissues or organs, rate regulation is developed as a special function of a certain cell or cells. The vagus and sympathetic are rate regulators of the heart. The sleep centre is presumably a specialized nervous structure which helps to regulate cerebral rhythms. The activity of nervous tissue is of course related to physico-chemical changes in the body. In our opinion, in epilepsy certain of these rate-regulating mechanisms are defective. Normally

the rhythm of the cortex is so well conditioned that there is only slight variation in frequency or in amplitude during the waking state.

As regards frequency regulation, the brain may be likened to a motor car which is being driven along a road with a ditch on the right called the *too slow* ditch and a ditch on the left called the *too fast* ditch. The

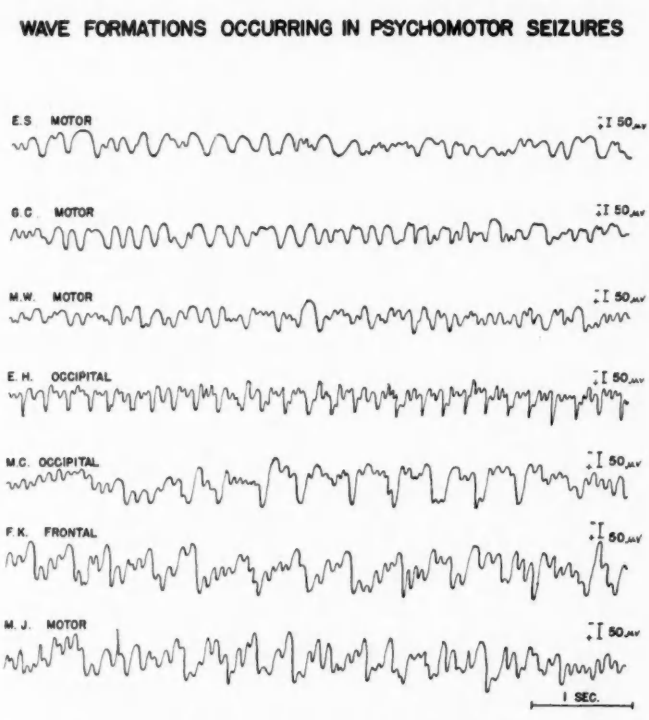

FIG. 2.—The electrical activity of the cortex during psychomotor seizures (7 cases).
The distinguishing feature of these records is the presence of many high voltage rather square-shaped waves with a frequency of from 3 to 7 per second. The patient whose record is labelled E. S. had a seizure in which she cried, "I am having the heart scared out of me," and would let no one touch her. G. C. mumbled, flexed her arms and legs and attempted to get out of the chair. M. W. cried, "I can't stand it," and began to tear her clothes. E. H. grumbled about his boss, dropped his pipe from his mouth, lit a match and tried to pull the electrodes off his head. M. C. repeatedly said, "Where is my pocket book." F. K. mumbled incoherently, tore up a letter and tried to eat it. M. J. groaned repeatedly and tried to pull the electrodes off his head. In all seizures there was anxiety and negativism with appropriate but poorly co-ordinated movements.

rate-regulating mechanisms of the brain normally steer along the centre of this road, but when these mechanisms are out of order they steer the brain first to one side and then to the other. The more defective the

steering (rate-regulating) mechanism the less quickly are deviations from normal corrected. *Petit mal* is an example of a minor disorder of rate-regulation in which the brain swerves quickly back and forth between too fast and too slow. In *grand mal* the rate regulators are so completely defective that the brain plunges far over to the too fast side, stays there for a considerable time, then goes over to the too slow side and remains there for a considerable time. In status epilepticus the brain goes through a number of these excursions to the fast side and then to the slow side before regaining its normal position with respect to frequency. In psychomotor epilepsy (psychic variants) the rate is abnormally slowed (fig. 2).

NORMAL AND EPILEPTIC DECELERATION OF CORTICAL ACTIVITY

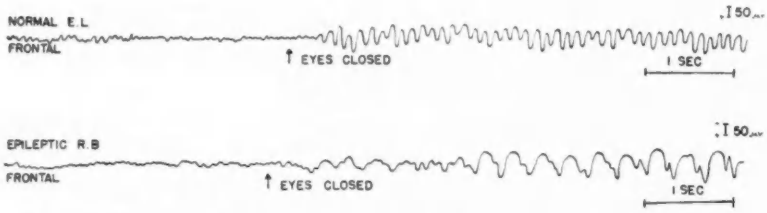

FIG. 3.—An example of the "overshooting" of electrical activity to which epileptics are liable.

In many normal subjects closing the eyes slows the cortical rhythms to approximately 10 per second, as is shown in the strip marked E. L.

The defect in rate regulation which is characteristic of epilepsy makes itself apparent in certain epileptics by extreme slowing of cortical rhythms when the eyes are closed. For example, R. B., a strip of whose record is shown in this figure, develops a steady 3 per second rhythm when the eyes are closed which soon shifts to a 3 a second wave and spike characteristic of *petit mal*. Such extreme slowing in a situation where slowing is normal is described as overshooting to the slow side. Overshooting to the fast side is also common.

Conditions such as excitement, closing of the eyes, or sleep, which modify the rate of the normal cortical rhythm, place a strain on the rate-regulating mechanisms of epileptics which they are frequently unable to meet (fig. 3). This we believe accounts for the tendency for seizures to occur on waking or on falling asleep. Seizures which follow emotional upsets (which cause moderate changes in rhythm even in normals) are often called "psychogenic." In general, electro-encephalograms made from time to time in epileptics show more variations than repeated electro-encephalograms of normal individuals.

(4) *Subclinical seizures.*—The electro-encephalogram often reveals

abnormalities of electrical activity which are not reflected in subjective or objective clinical manifestations. These abnormalities are of two types:—

First, the abnormal disturbance may be of the same pattern as found during clinical seizure, except much diminished in duration and in voltage. Subclinical *petit mal* attacks are more frequent than *grand mal*. They are seen usually in the records of patients with a history of very frequent *petit mal*. However, recorded *petit mal* lasting five, ten or fifteen seconds, may occur without clinical manifestations, and may be present in patients without a history of *petit mal*. For example,

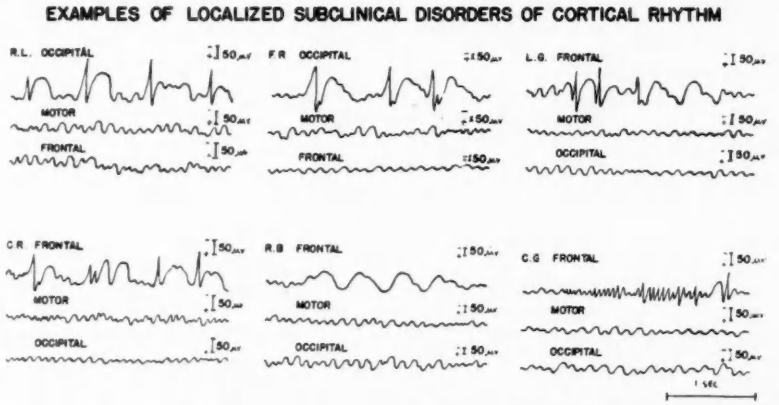

FIG. 4.—Six cases in which the electro-encephalogram gave evidence of a localized outburst of abnormal activity of the same type as was obtained from a wider cortical area at the time of a clinically obvious seizure. The localized disturbances shown here were unaccompanied by subjective or objective evidence of a seizure. The records marked R. L., F. R., L. G. and C. R., show activity of the *petit mal* formation. C. G. shows a crescendo burst of fast waves which are of the type seen in *grand mal*; following these there is a single *petit mal* formation.

one of our patients a man, aged 26, had a head injury in football four years ago. A year later he had a generalized convulsion, and in the last three years has had a total of six or eight attacks of *grand mal*. He is employed in posting quotations in a stockbroker's office, a job which requires continued alertness. Under close questioning neither he nor his parents gave any history of *petit mal*; yet when the record was made he was having *petit mal* attacks at the rate of one every minute. He was able to repeat numbers and to recall whatever was said to him during the period of electrical commotion which was taking place in his brain. Yet, when we requested him to perform problems in arithmetic, or to write sentences necessitating thought, he would hesitate in his

writing or in his speech when the abnormal cerebral rhythm occurred. He was not aware of anything amiss, and when his hesitation was pointed out, considered it a natural pause. Undoubtedly, *petit mal* occurs much more frequently than is realized. Especially is this true of *petit mal* which occur during sleep. In sleep they are never recognized clinically, yet may come more frequently than when the patient is awake.

The second type of subclinical disturbance is the presence of isolated abnormal waves of large voltage, occurring singly or in a short series. These may have the form of single sharp spikes, a spike and rounded hump, or square or round topped slow waves. Each is a component of a pattern which is characteristic for one of the three types of seizures. A patient who exhibits one of these isolated abnormal waves oftentimes has a history of that form of seizure in which such waves are evident. Such isolated abnormal waves are oftentimes confined to one area of the cortex (fig. 4). These large voltage waves are not to be confused with the continuous slow frequency waves five to eight a second) found in all leads of many seriously deteriorated epileptics. Whether irregularly appearing slow, large voltage waves are peculiar to persons with epilepsy is a question not yet answered.

(5) *Prediction of a seizure.—Grand mal* and psychomotor attacks can often be seen on the record a short time before there is clinical manifestation of the seizure. We believe it probable that close analysis of a patient's record, with attention to the predominance of certain slow or fast waves, will give warning for many hours of approaching *grand mal*. In one patient, daily records were made for 195 days and most of the *grand mal* which occurred in that period were correctly predicted (fig. 5).

(6) *The point of origin of the abnormal rhythm.*—So far, most of our work has been done with electrodes placed at different points on the scalp, and we can speak with assurance only of what takes place over the various readily accessible areas of the cortex. Abnormal rhythms commonly appear first in the frontal area, but frequently they appear first in the parietal or occipital areas. In several instances, the right or left frontal " fired off " before other areas and in a number of these cases, there was a definite history of trauma to this portion of the brain. In many patients, however, the abnormal rhythm appears simultaneously in all leads.

In a number of instances, the abnormal waves of subclinical seizures were entirely confined to a certain area. In these instances, it seems

that efforts at therapy might be directed at this particular spot. In one patient, we have made such a direct attack. This patient showed the wave and spike formation which is characteristic of *petit mal* only in the frontal areas, but each frontal lobe appeared to be independently

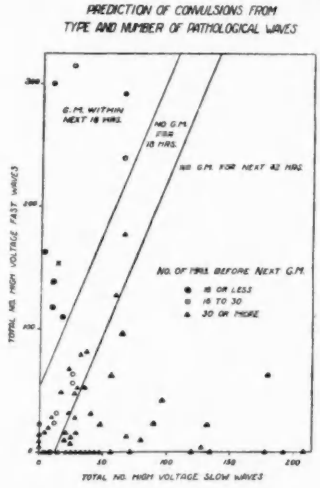
PREDICTION OF CONVULSIONS FROM
TYPE AND NUMBER OF PATHOLOGICAL WAVES
G. M. WITHIN NEXT 18 HRS.
NO G.M. FOR 18 HRS.
NO G.M. FOR NEXT 42 HRS.
NO. OF HRS. BEFORE NEXT G.M.
18 OR LESS
18 TO 30
30 OR MORE
TOTAL NO. HIGH VOLTAGE FAST WAVES
TOTAL NO. HIGH VOLTAGE SLOW WAVES

FIG. 5.—Prediction of convulsions from type and number of pathological waves in patient C. G., who has very frequent *petit mal* and occasional *grand mal*. Based on data obtained from analysis of a 15-minute record taken daily for 166 days, the abscissa represents the total number of high-voltage slow waves in the 15-minute record, and the ordinate the number of high voltage fast waves (spikes) in the same interval. Each symbol represents the record for a day. The symbol used varies with the number of hours after the record was made when the next *grand mal* occurred; a solid circle if less than eighteen hours, an open circle if from eighteen to thirty hours, and a triangle if more than thirty hours. The days in which the record was entirely normal are not charted. They were never followed by *grand mal*. If on a given day there were many high-voltage fast waves and few high-voltage slow waves, a *grand mal* seizure was imminent. If there were many high-voltage slow waves and a few high-voltage fast waves the patient was safe for a time. When there were few of both a seizure might be impending but was not imminent. The symbols represent what actually occurred, the diagonal ruling indicates the approximate prediction which could be made for the future. In the area marked *Grand Mal Within 18 Hrs.* there were three days on which a *grand mal* did not occur before eighteen hours had elapsed (two open circles and a square), on the day marked by the square. Double the usual dose of phenobarbitol had been given (for the effect of bromide in this case see fig. 6). In the area marked *No Grand Mal for 18 Hrs.* all predictions were correct; it contains only open circles and dots, the dots indicating that no seizure occurred for at least thirty hours. In the area marked *No Grand Mal for 42 Hrs.* records were characterized by very few high-voltage fast waves and numerous high-voltage slow waves. An actual record of this patient is shown in the frontal tracing of C. G., fig. 4. There are in this short space a dozen high-voltage fast (sharp) waves and one high-voltage slow wave.

affected. He had enostosis of the frontal bones by X-ray, and an atrophic appearance of both frontal lobes was found at operation. The anterior third of both frontal lobes was amputated by Dr. Jason Mixter. Since the operation, the abnormal wave and spike formations from the frontal

areas (but not his normal cortical waves) have almost disappeared. *Grand mal* attacks have been reduced to a very small fraction of their former number and psychomotor outbursts, which were the most distressing aspect of the case, have ceased. In addition, the patient is more alert mentally than before his frontal lobes were removed.

(7) *Visualization of the effect of treatment.*—In the case of patients having very frequent abnormalities of rhythm, a few hours' observation will determine whether the condition is improved or made worse by a given drug or treatment. Thus, we find that *petit mal* rhythms may be precipitated by a short period of overventilation and may miraculously

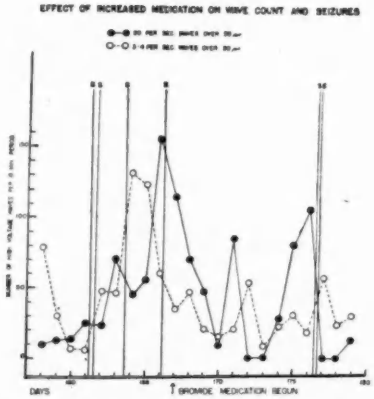

FIG. 6.—The effect of bromide medication on the incidence of seizures and on the number of high-voltage fast waves and high-voltage slow waves in a daily 15-minute record (Patient C. G.).

This is a continuation of the daily observations represented in fig. 5, except that the day-to-day changes can be followed by means of curves. The ordinate represents the number of high-voltage waves (either fast or slow) in the 15-minute record. The solid circles are the number of fast waves (20 per second) and the open circles the slow waves (3 to 4 per second). The perpendicular lines indicate the day and approximate hour when convulsion occurred. The patient had been taking daily small doses of phenolbarbital. After the 167th day she was given calcium bromide, 60 to 80 gr. daily. Experience based on the analysis of the previous 166 daily records of this patient indicated (*see* fig. 5) that when the number of fast waves greatly exceeded the number of slow waves the patient was due for a seizure within eighteen hours. However, on five of the days, after bromide medication was started the fast waves were much more numerous than the slow waves and yet no seizure resulted. It was only when the slow waves decreased in number and the fast waves rose to a peak that the situation got too much for the bromide to control and two seizures occurred.

disappear while the patient is breathing air containing from 3 to 7 per cent of carbon dioxide. Abnormal rhythms are greatly increased by insulin and decreased by glucose.

Sedative drugs have a varying effect depending on the type of abnormal rhythm. The anti-epileptic drugs, phenobarbital and bromide,

given in large doses intravenously while the record is being made cause a decrease in the rate of cerebral rhythms. These drugs are, therefore, valuable in conditions of abnormally fast rate, namely, *grand mal*; they may or may not favourably effect *petit mal*; and they actually accentuate the slow waves of a psychomotor disturbance. These laboratory observations are in agreement with our clinical observations. More than once we have unwittingly precipitated psychic episodes in patients subject to them by the intravenous injection of 10 gr. of phenobarbital sodium.

Although records of patients who are taking phenobarbital or bromide cannot be distinguished from the records of patients who are not, careful analysis of the record of a patient having frequent abnormalities will show the effect of the drug on his abnormal rhythm. If such a rhythm is a fully developed subclinical seizure, intravenous injections of bromide or of phenobarbital may inhibit or disorganize the rhythm. If there are isolated large spikes and large slow waves, the drugs may alter the ratio of their frequency.

The manner in which increased sedation effected the pathological activity of the cortex in one patient, who is subject to both *grand* and *petit mal*, is shown in fig. 6. In this patient a high ratio of large voltage fast to large voltage slow waves signalled an approaching *grand mal* seizure. When not taking bromides a convulsion was always followed by a sharp decrease of large voltage fast waves (spikes). The use of bromides seemed to raise the seizure threshold and did not permit so complete a discharge of *grand mal* activity, for when bromide was being given the fast waves decreased only slightly after a convulsion and then increased again rapidly so that the patient soon was having seizures as frequently as ever.

In addition to artificial means of inducing or of modifying the abnormal rhythms of epilepsy, we have observed that normal mental activity tends to inhibit, and unpleasant emotional states to augment, the frequency of *petit mal* rhythms. The clinical implications of these observations are obvious.

Conclusions.

The electro-encephalogram demonstrates the pathological physiology of epilepsy to be a paroxysmal cerebral dysrhythmia.

On the basis of some 900 hours of records obtained from a group of 400 epileptic patients, of whom 120 had from one to hundreds of seizures while the record was being made, we have secured the following data concerning epilepsy:—

(1) Seizures involving the cortex are accompanied by distinct and characteristic fluctuations in the action potentials of the brain.

(2) The rhythm which obtains during seizures is distinctive for the three main types: *grand mal* has a fast, psychomotor attacks (psychic variants) a slow, and *petit mal* an alternating fast and slow rhythm. The exact pattern of the seizure tends to be characteristic for each patient.

(3) Antecedent to these gross abnormalities of rhythm is the lack, in epileptics, of a competent control of cerebral rhythms.

(4) Some patients have subclinical seizures, which are typical short disturbances of rhythm not attended by subjective or objective evidence of a seizure. *Petit mal* may occur during sleep.

(5) There is evidence that *grand mal* may be predicted many hours in advance.

(6) In some patients abnormal activity begins in one area of the cortex and spreads to involve other areas. One patient with abnormal spikes confined to the frontal area has greatly improved following bilateral amputation of his frontal lobes.

(7) Electro-encephalography has been found useful in determining the value of various methods of therapy without having to wait for clinical seizures. Because anti-convulsant drugs slow cortical rhythms, they are more effective in *grand mal* than in other types of seizures. The inhalation of carbon dioxide and the administration of glucose are effective in temporarily abolishing certain abnormal rhythms. In some patients attention prevents the development of abnormal rhythms.

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SOMATIC MOTOR AND SENSORY REPRESENTATION IN THE CEREBRAL CORTEX OF MAN AS STUDIED BY ELECTRICAL STIMULATION.[1]

BY WILDER PENFIELD AND EDWIN BOLDREY (MONTREAL).

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(1) Introduction.

Recent experimental work on the localization of motor function in the cerebral cortex has spurred us to make a complete analysis of the records of our patients (163 in all) upon each of whom we have carried out electrical exploration of the cortex under local anæsthesia.

[1] From the Montreal Neurological Institute and the Department of Neurology and Neurosurgery of McGill University, Montreal. Read before the American Neurological Association, Atlantic City, June 4, 1937.

This has led us to conclusions which differ somewhat from those published by other observers in regard to the localization both of sensory and motor function. Often we have found it impossible to confine functional representation within strict cytoarchitectural boundaries. The human cortex shows definite differences from that of other mammals and human pathological processes introduce important new elements.

(2) Historical Note.

Flourens (1842) carried out experimental removals of areas of brain and concluded that up to a point any part of the cerebral hemispheres could quite adequately exercise the function of the whole. This attitude, which bears some resemblance to that recently adopted by Lashley (1929) was considered to deny the possibility of circumscribed localization of function in the brain.

Broca (1861) gave the most effective impetus to the search for localization of function when he described an area of the left hemisphere of man as a specialized speech centre. Hughlings Jackson (1864) noted an association between speech defect and right sided chorea, saying that he saw "no more difficulty in supposing that there are certain convolutions superintending those delicate movements of the hands which are under the immediate control of the mind, than that there is one, as Broca suggests, for movements of the tongue in purely mental operations."

To Fritsch and Hitzig (1870) must be given credit for the first successful, controlled direct electrical stimulation of the mammalian cerebral cortex. By applying galvanic current through bipolar electrodes to the anterior half of the dog's hemisphere they obtained movements of muscle groups in the opposite half of the body. From the posterior part of the brain they secured no motor movements. Their map contains five motor points. Jackson was jubilant at this verification of his hypotheses and said (1873) the work of these experimenters demonstrated " that discharge of convolutions develops movements, notwithstanding that destruction of limited parts of the brain produces no obvious loss of movements."

Ferrier quickly took up the work in England and in 1876 published the results of repeated cortical stimulation in several species. Using a faradic current he obtained movement from points behind the Sylvian fissure, results which were roundly criticized by Hitzig. Nothnagel (1873), Hitzig (1874), Schiff (1875) and Hermann (1875) thought that the cortical centres were really sensory centres for " muscle sense," to use the words of the first two.

Dupuy (1873), Sanderson (1874) and Carville and Duret (1875) agreed that spread of current, principally to subcortical centres, accounted for the movements recorded. With this Ferrier (1876) could not agree, but he did admit that motor response might be an expression of sensation and that the character of the sensation might determine the nature of the movement. Although their work dealt chiefly with cortical removals, Luciani and Tamburini (1879) and Munk (1890) added confirmatory evidence to the sensorimotor conception of the Rolandic area.

In 1888 Dana reported 142 cases of sensory disturbance in man associated with cortical paresis. He observed that all cases of cortical anæsthesia were associated with some amount of paralysis.

Horsley and his collaborators conducted a minute examination of the motor area in apes. Beevor and Horsley's map of the cortex (1890) showed that there were motor points anterior and posterior to the Rolandic fissure, and overlapping of cortical areas. Bilateral innervation, they found, was confined to mouth and throat movements. In the higher apes they found inexcitable spaces among the normal areas of the pre-Rolandic cortex.

In 1894 Mott summarized the attitude of the three camps with divergent views on Rolandic cortex function. Ferrier, Schafer and Horsley believed the area to be purely motor. Schiff was certain it was purely sensory. Hitzig, Bastian, Bell, Wundt, Hughlings Jackson, Munk, Tripier, Luciani and Mott would call it sensorimotor. Sensory information in animals, of course, could be obtained only by extirpation experiments. Although it was not then clearly established, the idea of a sensorimotor cortex was generally held.

It was the work of Grünbaum and Sherrington (1901, 1903) which, according to Dusser de Barenne (1935), caused the change of opinion from the idea of sensorimotor cortex to the conception of a pre-Rolandic motor cortex separate from the sensory region. They worked with a unipolar electrode using weak currents to avoid seizures. The animals, however, were under general anæsthesia. In anthropoids, under those conditions, they found the excitable cortex to be limited to the precentral gyrus (fig. 1). This gyrus in anthropoids contains Areas 4 and 6.

In no case did they find primary motor response postcentral to the fissure of Rolando. They obtained discrete movements of ear, nostril, palate, lips, jaws, vocal cords, chest and abdominal wall, pelvic floor, anal and vaginal orifice as well as of the extremities. They found the

insula to be inexcitable even with strong currents and were unable to obtain vocalization. Conjugate movements of the eyes to the opposite side were obtained by stimulation in the frontal lobe and the occipital pole in regions (fig. 1) which must have corresponded roughly to Area 8 and Area 17 of Brodmann. Grünbaum and Sherrington found that postcentral removal produced no paresis and precentral extirpation caused a severe, but rapidly diminishing paralysis of the movements which electrical stimulation of that area had previously produced. They

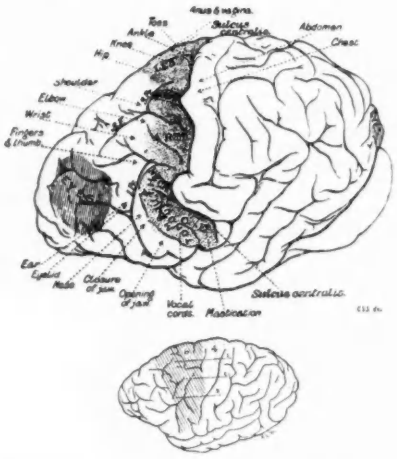


FIG. 1.—Results of cortical stimulation in the chimpanzee above (from Grünbaum and Sherrington, 1901). Cytoarchitectural localization of Areas 4 and 6 in the chimpanzee below (from Bucy, 1934). Comparison of the figures indicates that the isolated movements found by Grünbaum and Sherrington were not confined to Area 4 in the arm and face areas. Eye movements only were found from the detached frontal lobe centre. The same was true of the occipital centre for eye movement. Movement points end abruptly at the central fissure.

observed that the response from a cortical point might be "influenced by the particular forms of movement excited from neighbouring points just antecedently." They pointed out that a cortical point was, therefore, to some extent unstable and that by preliminary precentral stimulation a response from the post-central gyrus could be elicited. This process they called "facilitation." Graham Brown alone and with Sherrington followed up this problem at a later date (Brown, 1915, 1916), and showed that a spot stimulated might be sensitized by facilitation and that an echo response of secondary facilitation might be produced in a neighbouring point in the postcentral gyrus (activation). Furthermore, Graham Brown and Sherrington showed that a response might

be qualitatively changed, i.e. from flexion to extension. This they called " reversal."

O. and C. Vogt combined careful cytoarchitectural studies with animal stimulation and produced for the monkey a map which resembles those of Grünbaum and Sherrington. By means of their cyto-architectural studies of the human cortex they prepared a map of the human cortex and transferred functional localization points to it (1926). This map (fig. 2) corresponded to an extraordinary extent with that which

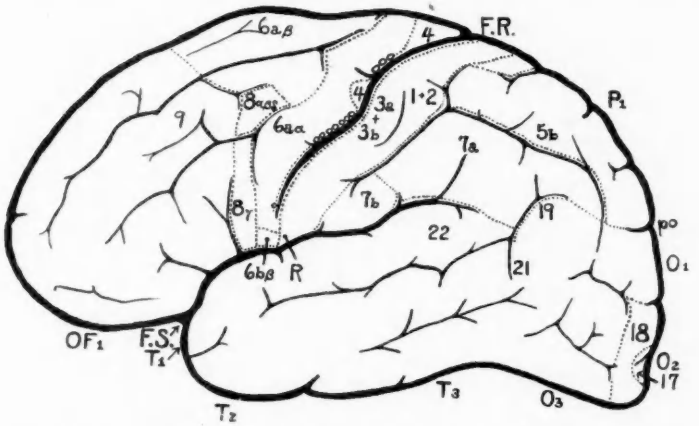


FIG. 2.—Cytoarchitectural fields of human cortex after Vogt and Vogt (1926). The functional interpretation is deduced by them from the homologous fields in monkey. F.R. = fissure of Rolando. F.S. = fissure of Sylvius. p.o. = parieto-occipital fissure. R. = respiration. 4 = true pyramidal cortex or "primary field for tonic specialized movement." 6*a alpha* = "secondary field for tonic specialized movements" which acts upon the primary field by conduction along the outermost layers of the cortex; 6*a beta* = tertiary field where stimulation most easily causes turning of eyes, head, ears and body to opposite side (adversive movements); stronger stimulation gives movements of both upper and lower extremities; 8 *alpha, beta, delta* = field from which adversive eye movements were most easily produced; field 3*a*, 3*b*, 1 and 2 = postcentral convolution producing movement by action upon field 4. 5*b*, 7*a* and 7*b*, all produce adversive movements with strong stimulation; 19 (also 17 and 18) = adversive eye movements: 22 = ear and eye adversive movements; 6*b* = mastication.

Foerster prepared for man as the result of stimulation of patients, as indicated in the Vogts' publication just cited.

Recently Fulton (1936) and his associates, working upon monkeys and anthropoids, and using the fields of Brodmann and Vogt (fig. 2), have urged that the motor representation in the cerebral cortex is made up of: (*a*) motor area or Area 4 of Brodmann which gives origin to the pyramidal tract; and (*b*) a " premotor " area made up of (i) Brodmann's Area 6*a alpha*, which together with Area 4, composes the precentral

gyrus in man; and (ii) Brodmann's Area 6*a beta* which in man lies anterior to the upper end of the precentral gyrus. Fulton used the term "extrapyramidal" motor cortex to indicate all of the cortex which might be motor in addition to Area 4.

The evidence from the study of human cases may be summarized as follows:—

Roberts Bartholow, an American surgeon of Cincinnati, is credited by Beevor and Horsley (1890B) with being the first to stimulate the human brain directly. It is true that Hitzig (1870A) had preceded his animal experimentation by indirect galvanic stimulation of the occipital region of a man, thus producing eye movements. The account of Bartholow (1874) is interesting to say the least and may be cited.

His patient was a 30-year old-domestic. As an infant this unfortunate had chanced to fall into the fire, burning her scalp so badly that "hair was never reproduced." A piece of whale bone in the wig she was forced to wear irritated the scarred scalp and, by her statement, three months before she was admitted, an ulcer appeared. When she presented herself for relief, this had eroded the skull over a space 2 in. in diameter "where the pulsations of the brain are plainly seen."

Although "rather feeble-minded" Bartholow observed that Mary returned replies to all questions and no sensory or motor loss could be made out in spite of the fact that brain substance apparently had been injured in the process of evacuation of pus from the infected area. The doctor believed, therefore, that fine insulated needles could be introduced without further damage.

First he observed that no pain was experienced from the brain substance proper and that mechanical irritation yielded nothing. Faradization of the dura "with the least possible current" produced muscular contractions of the opposite arm and leg, and head turning to the opposite side.

One of the needles was then passed into "the left posterior lobe so that the non-insulated portion rested entirely in the substance of the brain," the other needle resting on the dura. There was produced a muscular contraction of the right upper and lower extremities with "faint contraction of the orbicularis palpebrarum and dilatation of the pupils." She also complained of a "strong and unpleasant tingling in both opposite extremities, especially the arm, which she seized with the opposite (left) hand and rubbed vigorously." A similar manœuvre on the right side produced similar results.

While the electrodes were in the right side Bartholow decided to try the effect of more current. "Her countenance exhibited great distress and she began to cry. Very soon the left hand was extended as if in the act of taking hold of some object in front of her; the arm presently was agitated with clonic spasms; her eyes became fixed with pupils widely dilated; the lips were blue and she frothed at the mouth; her breathing became stertorous, she lost consciousness and was violently convulsed on the left side. This convulsion lasted for

five minutes and was succeeded by coma. She returned to consciousness in twenty minutes from the beginning of the attack and complained of some weakness and vertigo." Three days after this stimulation, following a series of right-sided seizures, the patient died.

Sciamanna's results in 1882 were similar (see Beevor and Horsley, 1890B). Horsley (1887), Keen (1888), Nancrede (1888), Lloyd and Deaver (1888), Parker and Gotch (1893) and Bidwell and Sherrington (1893) corroborated in the human the motor responses previously obtained from the motor cortex of animals. In 1892 Ransom stimulated the cortex of a conscious patient and produced both sensation and movement.

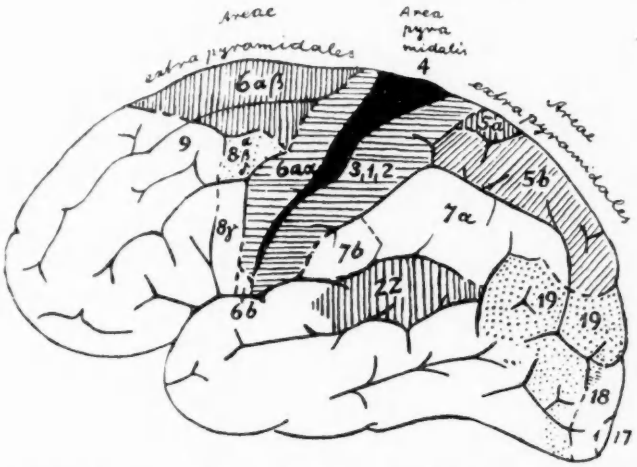


FIG. 3.—Extent of motor cortex in the human brain, after Foerster (1936). The cortical areas for motor response to electrical stimulation are outlined. The numbers refer to the cytoarchitectural fields of the Vogts described in fig. 2. Mass movements and adversive movements are reported from the extrapyramidal areas including 6*a beta*, 5 and 22. Movements from the pyramidal area are distinctly isolated in character. The extrapyramidal system produces mass movements of the opposite side, according to this author.

Cushing (1909) was the first to produce sensation without movement in man. He stimulated the postcentral gyrus of two conscious patients each of whom reported sensations in parts corresponding with areas where movement could be produced from analogous precentral regions. Van Valkenburg (1914) corroborated these findings.

Foerster (1936A and B), as the result of stimulating the human cerebral cortex, chiefly under local anæsthesia in cases of focal epilepsy, widely extended the motor cortex (fig. 3). He pointed out that the "precentral areas are chiefly motor and the postcentral convolution is

chiefly sensory," but he included the postcentral convolution as motor in a sort of secondary category.

In general agreement with Fulton, Foerster added a frontal extra-pyramidal motor area ("6*a beta*"), a parietal extra-pyramidal area ("5") and a temporal extrapyramidal area ("22"). He stated that even in the absence of the pyramidal zone 4 these areas (as well as Area 6) were capable of producing a mass movement of the opposite side of the body when stimulated strongly by a faradic current. In the intact brain the post-central gyrus was able to produce isolated movements with a higher threshold than the precentral, but when Area 4 was absent this response ceased and only the mass movement described above was produced.

(3) Clinical Material.

The observations reported here were made during operations carried out since 1928 by one of us (W.P.).[1] Of the 163 operations in which cortical stimulation was carried out, 126 proved to have records suitable for the present analysis.

In general, stimulation was only carried out in any operation when there was therapeutic justification for it. In some instances it was used to define the motor area of the hemisphere so that an infiltrating tumour could be removed as widely as possible without producing paralysis. More frequently stimulation was made use of as a preliminary to radical extirpation of an epileptogenic focus and as an aid in searching for that focus. The actual therapeutic results of such operations are completely summarized elsewhere (Penfield, 1936).

However, in the therapeutic approach, it should be pointed out that only very rarely has the Rolandic area been included in any excision and never has this region of the brain been touched unless a lesion was present that could be demonstrated grossly by operative inspection. This digression is made in the hope of discouraging surgical removal of normal brain from the Rolandic area, or elsewhere, whatever may have been the pattern of epileptic seizure.

The operations have been carried out as follows:—

Sterilization of scalp: local injection of nupercaine in solutions of 1 : 1,500 and 1 : 4,000 to which adrenalin is added. The sterile towels are then arranged perpendicularly so that the patient is cool, can see and move freely, and can be observed constantly. The rôle of anæsthetist is most important even though

[1] Thirteen of the reported operations were carried out by our associate Dr. William Cone and are included here by his kind permission.

a general anæsthetic is rarely given, and in all of the records found in this communication we are indebted to our anæsthetist, Miss Mary Roach, who constantly followed the behaviour and movements of the patients as well as their blood-pressure, pulse and general condition through the long and sometimes trying ordeal of electrical exploration of the cerebral cortex.

Osteoplastic craniotomy is used to expose large areas of the hemisphere, and the bone is replaced at the close of operation. The exposed brain is kept warm by the heat of lights focussed upon it, and moistened with Ringer's solution applied with an atomizer.

Stimulation is carried out by either unipolar or bipolar platinum electrodes which emerge from a glass handle and are attached to insulated wires, all of which may be autoclaved. Formerly we used a galvanic current for localizing purposes and a faradic coil to induce seizures. In recent years we have found a thyratron stimulator, similar to that described by Schmitt and Schmitt (1932), much more satisfactory and have usually employed a wave frequency of from 55 to 65 per second. This instrument is to be found now in use in physiological laboratories. It produces a current which resembles the faradic current of an induction coil, but here the thyratron tube filled with mercury vapour acts as the interrupter. The current is thus constant and may be altered accurately in rate and intensity.

It is essential that the patient should be in sympathy with operator and anæsthetist, and it is an interesting comment on the bravery and fortitude of mankind that almost without exception these subjects have gone through the ordeal of operation patiently and intelligently, even when young children. But however great may be their power of introspection, we make it a rule to restimulate all doubtful points without warning. Responses which cannot be reproduced, especially unusual ones, are eliminated.

Beginning with a subliminal stimulus, the strength is increased until a positive response is obtained. The threshold of the postcentral convolution is usually below[1] that of the precentral, although they are often the same. It is usually best to outline the Rolandic fissure thus before exploring further. Each time a positive response is obtained a small square of paper bearing a number is placed upon the brain at that point. These numbers or letters, beginning at 1 or A, indicate the order in which positive responses were obtained.

After outlining the fissure of Rolando the intensity of current is then increased and exploration carried further afield over the cortex. No record of the position of negative stimulations is made.

Details of the electrical exploration are recorded by a running dictated description from the surgeon to a stenographer who is present at this stage of the operation. She records the number of the stimulation, description of the response and the time of each. Photographs are taken in a camera outside the operating theatre through a mirror placed above the operating table (described

[1] Foerster has found the reverse to be the case.

by Hayden, 1936). The surgeon, with sterile paper and pencil, also makes a sketch at the close of stimulation, placing the numbers where he thinks they should fall upon a uniform life-size brain diagram like that employed for the charts in this communication. On this sketch he measures the distance from central fissure and from the fissure of Sylvius for each number.

(4) Method of Analysis.

Auditory, visual and olfactory responses have been eliminated from this report. Analysis of the drawings, photographs and operative notes has been made by one of us (E.B.) as follows:—

A separate summarizing chart was made for each individual movement or sensation produced by stimulation. For example, all movements of the thumb obtained by stimulation in the right hemisphere were placed on one chart with the reference number of each case. Movements of the thumb from the other hemisphere were first charted separately in like manner, and the index finger and other members similarly. When found to be alike the results from the two hemispheres were then combined for each member. Unilateral and bilateral responses were separately recorded.

Each operation in the series was given a number, and as the results were transferred from the operation records to the summarizing charts the operation number was placed beside each of its points, thus making it possible to refer back from the common movement or sensation chart to the operation report if desired. No movement or sensation which was part of a definite epileptiform seizure has been included here as a sensory or motor phenomenon.

In transferring the stimulation points they have been placed on the common chart by reference to photograph and sketch according to their distance from the Rolandic fissure. From above down the points were placed in proper orientation according to the distance from the Sylvian and the median longitudinal fissures. These are the only landmarks on the brain surface which can be recognized with any degree of accuracy. Indeed, the Rolandic fissure can hardly be recognized until after stimulation has identified it. Estimation of position was necessary in a few of the earlier drawings. In the large majority of instances, however, direct measurements and photographs have made the exact topographical localization of the points as accurate as is possible.

In this way 170 summarizing charts were made which have been condensed into the sixteen illustrative charts reproduced here. All results have been transferred to the right hemisphere for the sake of uniformity and brevity.

(5) Illustrative Case.

One operation record may be described here in detail as an example:—

Case 110.—M. G., a girl aged 21, suffering from Jacksonian seizures beginning with a sensation in the left hand. Right osteoplastic craniotomy; nupercaine analgesia, June 9, 1936. An area of abnormal brain was excised,

the area being quite small and limited almost altogether to the postcentral gyrus. The procedure has not, alas, resulted in cessation of attacks. The report follows.

"*Objective Findings.*—The dura was under slightly increased pressure and the bone was unusually indurated. There was a scalp scar in the posterior parietal region and a great deal of thickened tissue underneath the scalp, showing that there had been a considerable subaponeurotic hæmorrhage at some time or other. The brain seemed to be normal excepting that the gyri in general were a little small. It was noted that one gyrus was slightly yellow and somewhat flattened and that just below this yellow area the gyrus was extremely narrow; this proved, on stimulation, to be the postcentral gyrus and the actual focus from which the attacks were coming. The extreme narrowing seemed to be slightly below the focus from which the attack could be produced and the narrow area corresponded with the letter "K" which produced sensation in the thumb and running over toward the index finger. This was the most satisfactory response as far as postcentral gyrus was concerned."

"I think that even a greater subdivision of responses could have been obtained if time had been available. The same weak strength of stimulation, namely 24, was used all along the motor gyrus without producing any tendency toward an attack. The three attacks were all produced within a short radius in the abnormal convolution."

"*Procedure.*—A moderate sized osteoplastic flap was turned down posteriorly, the dura was opened and after the electrical exploration an oval incision was made in the brain about the epileptogenic focus. Cutting with thread, the incision was carried down to a depth of about 1½ cm. It was noted that after the threads were tied, outlining the block to be excised everywhere except at the bottom, there was no reduction in the strength of her grip; this in spite of the fact that the area must have been cut round quite well. After removal of the block of tissue, however, she lost almost complete use of her hand." (See dictated note below.)

"The removal was practically all postcentral but it must be noted that there was some injury to the precentral gyrus but not to a depth of greater than 2 to 3 mm. and over an area not greater than 1 cm. in length. All devitalized tissue was removed. The dura was closed excepting under the temporal muscle where a small decompression was left. The bone flap was fastened with steel wire at two points mesially and left free below. The aponeurosis and skin were sutured by Dr. Walker."

Dictated Record of Stimulation.

(Stimulating thyratron intensity 30, raised to 24 from B on: frequency about 65, bipolar electrode; letters and numbers laid on brain as shown in fig. 4. The following record is given as dictated but quotation marks are used only to signify the patient's own words.)

Four negative stimulations.

A. Pain in right side of face; unable to secure this from dura adjacent.

Repeated twice—failed twice, should be ignored.
Two negative stimulations.

B. Arm and hand "feels as though it was going to sleep."
Repeated once without warning.

C. Numbness left side above umbilicus. This location seems to be epigastric.

D. Sensation in right arm and hand; when repeated, said to be more in arm.

E. Sensation in hand and fingers; when asked what the sensation was like she replied: "like going to sleep." When asked if it was numbness or tingling, she replied "Both."

F. Sensation in ring and little finger.

G. Sensation in same fingers.

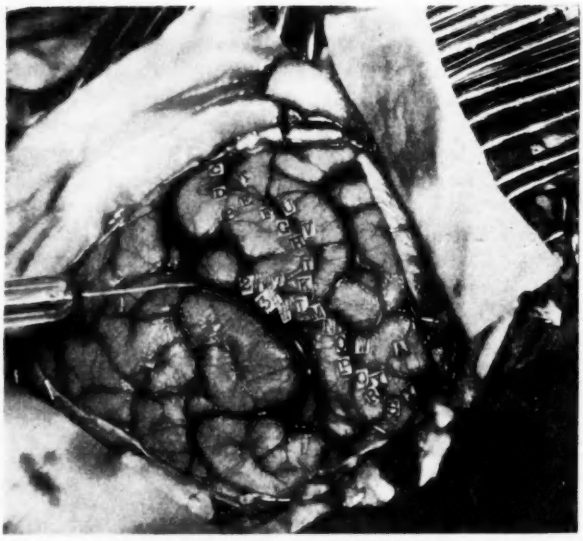


FIG. 4.—Cerebral cortex in Case 110 photographed during operation. The tickets of reference indicate responses which are described in text. *See* fig. 24 for diagram of same case.

Changed from Bipolar to Unipolar Electrode.

11 a.m. Left leg "going to sleep"—no stimulation.

H. Same feeling in index and large fingers.

I. Sensation in index finger—same feeling.

K. Sensation in thumb.

L. Sensation in thumb and toward index finger, but not in that finger.

M. Sensation left side of face—numbness.

N. Patient laughed a little; sensation in lower left lip.

O. Lower lip, left side.

P. Upper and lower teeth and gums.

Q. Left side of tongue and tip.
R. Tip of tongue, left side.
S. Back of left side of tongue.

Three negative stimulations.

T. Marked flexion of forearm on arm.
Repeated—no sensation. Same just above "T."
U. Inward rotation of hand and arm and slight flexion of fingers.
Indefinite sensation of numbness in hand and fingers.

One negative stimulation.

V. Slight flexion of hand and fingers; no sensation.

Two negative stimulations.

W. Mouth drawn to left and downward; no sensation.
X. Tongue drawn downward and to left; no sensation.
Y. Tongue drawn to left; movement of neck to left.
No response between "V" and "W."

Two negative stimulations.

11.10 *a.m.* *Attack following stimulation at* ⁋.—Patient said she had sensation in the left thumb; next that it was going to the hand: next up the arm. Then convulsion characterized by slight convulsive movement of left hand and arm. Her first observation at the end was "Did he see it? I have had an attack." Pulse at wrist present throughout attack. Slight confusion at close and restlessness. No clonic movements elsewhere. Duration from sensation in fingers to her question after the attack was 1 min. 54 secs. In the brain it was observed that the hemisphere as a whole was pulsating during the attack. At least one artery was observed not to be pulsating during the attack. This artery showed visible pulsation at the close. An artery further posterior was also seen to begin to pulsate at the close of the attack.

11.17 *a.m.* *Attack* 2.—Patient was silent. Change in circulation of brain was noticed and spoken of before we realized an attack was starting. I do not know how to describe the alteration. A few seconds later Miss Roach stated that an attack was beginning. Brain then bulged and for a few seconds there was no pulsation in the cerebral arteries. Pulsation in the arteries began before the end of the attack and the brain began to recede. Pulse was present in wrist all the time.

Patient was not conscious that she had had an attack but she remembered that she had had sensation in thumb and then that it was going to her fingers. Stimulation producing each of the attacks was no longer than one second. Three negative stimulations.

Z. Sensation in thumb.

Experimental activation (or secondary facilitation).—Stimulation on the anterior margin of the precentral gyrus at level of T in figure 4 gave no response. Stimulation at T gave marked flexion of elbow as previously. This stimulation was then followed at one second intervals

by a succession of stimuli which advanced anteriorly across the convolution to the anterior margin of the gyrus. Each stimulation was followed by elbow flexion of about the same intensity. This movement was thus produced from an area which had previously refused to give movement. The same thing was repeated in the postcentral gyrus. Thus a sensation in the arm was produced at D and reproduced by each successive stimulus back to the posterior margin of the gyrus, although there had been no sensation when the posterior margin had been previously stimulated.

Attack 3.—Same as time before. Did not know she had one. Followed by slight emotional change and flushing of face. There seemed to be a variation in pulsation of the arteries. Pulse felt in wrist continuously. Duration of third attack thirty seconds.

Examination following excision.—Immediately after all the cutting sutures were tied the patient was able to squeeze the dynamometer up to 13 with her left hand, while she could do it up to 15 with her right hand. After the extirpation, however, she could not squeeze the dynamometer at all although she was able to extend her wrist, just causing the hand to close a little. On leaving the operating room I found that pricking with a needle of any one of her fingers or thumb gave her pain and she was able to localize it to the proper digit. However, if any of the digits were pinched, moved or touched she had no intimation of it. She did not seem to know where her hand or arm was. On showing her teeth there was possibly a very slight weakness of the left side but nothing more than that.

(6) Topographical Analysis.

The responses for each subdivision of the body are analysed separately below and summarized in accompanying charts. Points which are widely displaced from their natural groupings can usually be explained by "epileptic spread" which will be discussed under a subsequent heading, or by the gross cerebral deformation due to a pre-existing lesion.

(7) Movements of the Tongue (fig. 5).

There are sixteen accepted points producing tongue movement in this series. Thirteen of these are precentral and three are postcentral. Ten points, including all of the postcentral ones, are from the left hemisphere. Because of the tongue's objective inaccessibility its movements can be discovered only through voluntary information from the patient, so that some movements may have been missed. For the same reason it was impossible in most instances to record the exact type of movement whether contralateral, ipsilateral, or bilateral.

Only point 44 is very far removed from the fissure of Rolando. This was the case of an epileptic who had a bilateral cerebral lesion. Point 18 from the same patient was found on the opposite hemisphere. On neither side did the point seem to be displaced by an "epileptic habit." Point 40 may perhaps have been displaced by the patient's lesion, an infiltrating glioma.

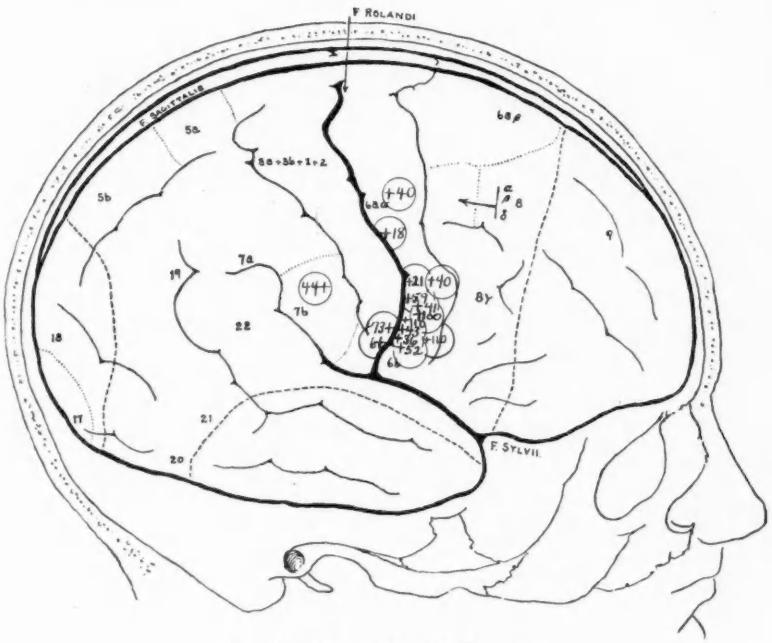


FIG. 5. — Movements of the tongue.

(8) SENSATION IN THE TONGUE (fig. 6).

Patients show great capacity for exact localization on the tongue. The information received has resolved itself into six groups listed as contralateral side, tip, middle, base, place not stated and taste. There is a total of 99 postcentral, 24 precentral, and 2 superior temporal points.

The sensation was recorded as contralateral side 48 times, of which 39 are postcentral, 8 are precentral and 1 is temporal. Twenty-three postcentral, 3 precentral and 1 temporal point gave sensation at the tip. There was feeling in the middle of the tongue during 8 postcentral and

4 precentral stimulations. Two postcentral and 2 precentral points gave a sensation at the base.

The exact point on the tongue was not stated in 33 instances, 26 postcentral and 7 precentral. In one instance only (postcentral) the sensation was on the ipsilateral side. Twice the sensation was that of movement. One precentral point gave a feeling of "inability to control my tongue."

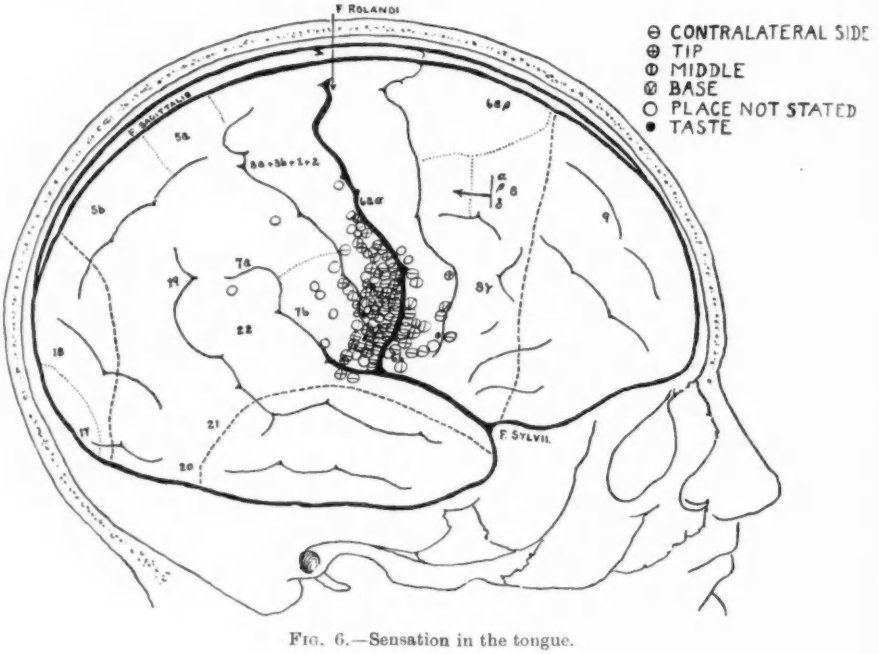


FIG. 6.—Sensation in the tongue.

In five cases the patient described the sensation as being one of taste. Four of these points were postcentral and one precentral. The particular kind of taste was not described. The two points beneath the Sylvian fissure were checked without warning with the same result.

The fact that points on the chart take up space gives the impression that the cortical points extend farther from the Rolandic fissure than is often the case. Usually the responsive areas were very near the anterior lip of the postcentral gyrus. It is obvious, however, that the region may extend one and one half centimetres behind the central sulcus and the same distance in front of it.

Bilateral and ipsilateral sensations are more frequently encountered in the tongue than in any other part of the body. In those cases, seven in all, where sufficient detail was available, it was found that the tip of the tongue had a position on the cortex above the side and base in five instances, and below the side and base in two instances.

(9) Movement and Sensation in the Mouth (fig. 7).

For the mouth and lips there are 3 postcentral and 18 precentral motor points to be compared with 21 precentral and 53 postcentral points for sensation. The sensations reported were described much as

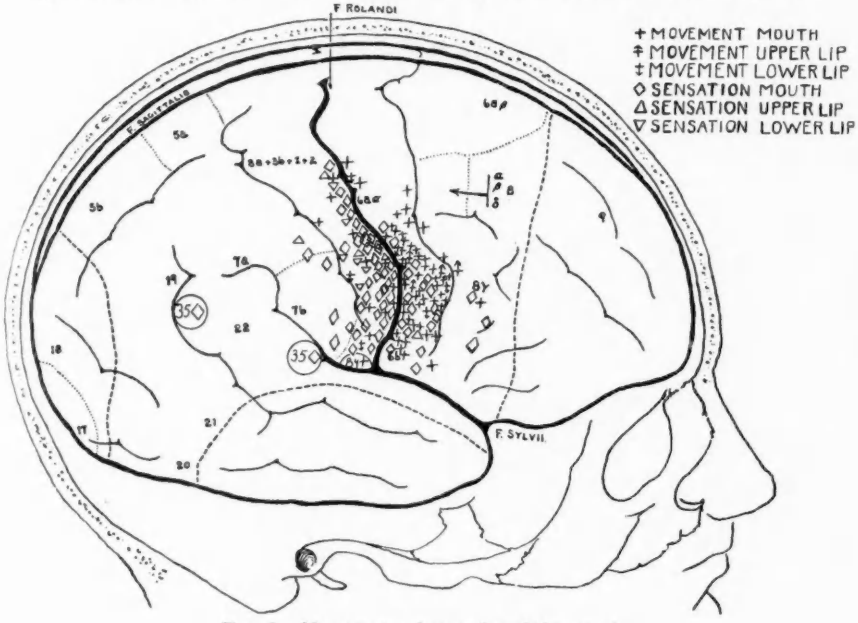


Fig. 7.—Movement and sensation of the mouth.

elsewhere, usually as tingling or numbness. Movements have been most often twitching in character, but also opening and closing, smacking, sucking and trembling of the mouth. Ipsilateral lip movement occurred eight times.

Special attention should be called to the comparatively large number of precentral sensory and postcentral motor points in this group. It is also of interest that the sensory localization extends farther, both anterior and posterior to the fissure of Rolando. Motor point 84 (near the inferior end of the postcentral gyrus) was the sole motor response from

this patient. Shortly before operation she had developed a hemiplegia following status epilepticus.

(10) Jaw Movement and Sensation within the Mouth (fig. 8).

For the purposes of this chart "in the mouth" means in the teeth, palate and jaws. There are 40 postcentral points and 16 precentral points which have produced such sensation. Ipsilateral feeling has been moderately frequent. One point gave a sensation of cold. None of these patients experienced pain in jaws or teeth, but usually numbness.

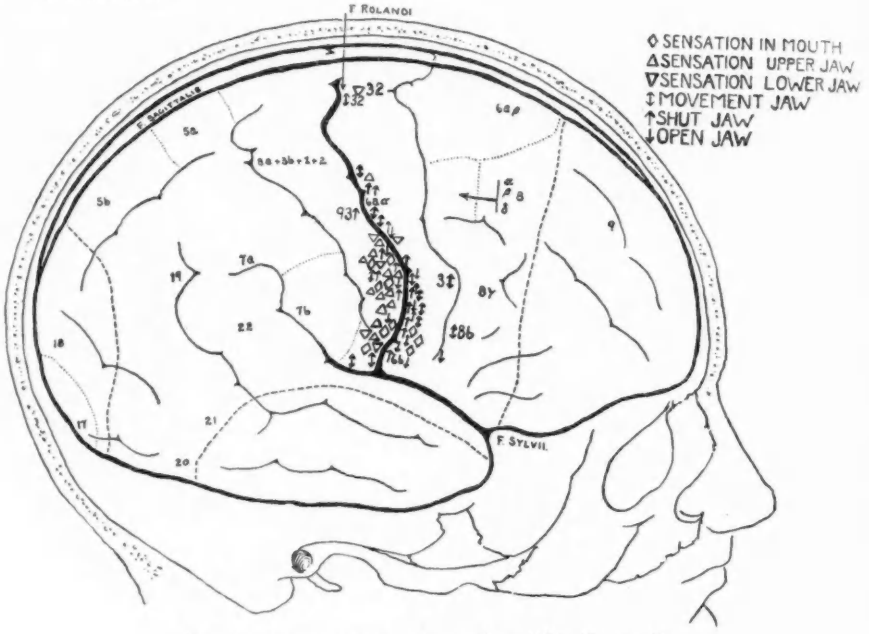


Fig. 8.—Jaw movement and sensation within the mouth.

Forty-one points produced jaw movement. Twenty-nine of these were precentral and the remainder were postcentral. Simple "jaw movement," which usually means opening and closing, occurred 25 times, 19 of which followed precentral stimulation. Six precentral and 4 postcentral points produced jaw closing; 4 precentral and 2 postcentral points produced opening of the jaws. With two exceptions all of these points are within a centimetre of the Rolandic sulcus.

The points 32 are obviously well away from the general centre.

The scar in this epileptic subject was over 4 cm. below and in front of these points. It is doubtless an example of displacement of response due to habitual epileptic discharge, a subject to be discussed presently.

(11) Movement and Sensation of Face (fig. 9).

The striking thing about this chart is the relative rarity of motor response from the postcentral gyrus as compared with other areas of the body. Thirty precentral and one postcentral points produced eyelid movement; of these, eyelid closing was the most frequent

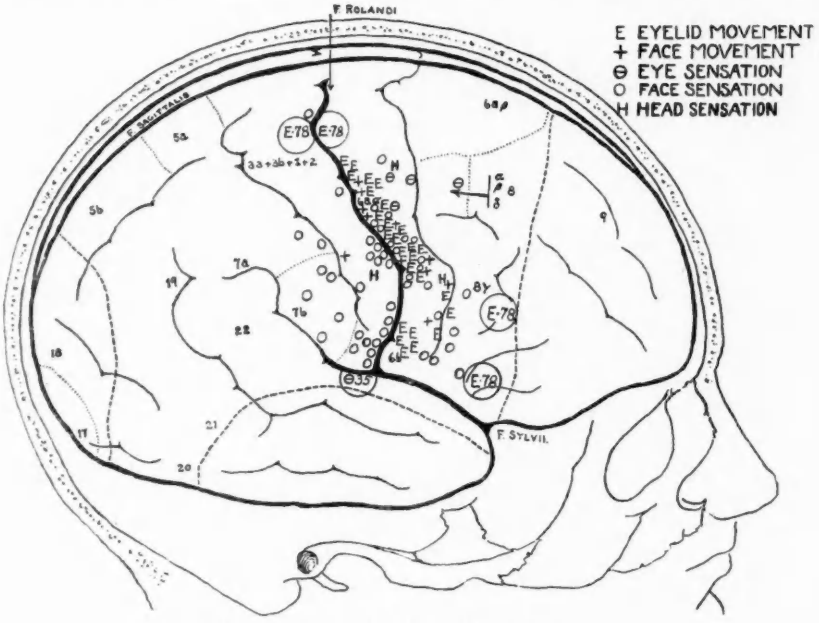


Fig. 9.—Movement and sensation of the face.

response. Other common movements were twitching and opening of the lids. Twelve other motor responses were simple "face" movements, usually twitches and including nose and brow. The four atypical points of case 78 were thoroughly re-checked. There were no other points in the vicinity which could give this response.

Somatic sensation in the eye occurred after four precentral and one temporal stimulation. Sensation in the remainder of the face was quite common. There are 20 precentral and 24 postcentral points on the

chart. There is a suggestion of a grouping of these face sensations at the inferior end of the postcentral gyrus.

One motor point in Case 118 produced elevation of the opposite brow, opening of the opposite eyelid and turning down of the corners of the mouth. This was not part of an habitual epileptic pattern. It seems to have been a grimace activated from a single motor point.

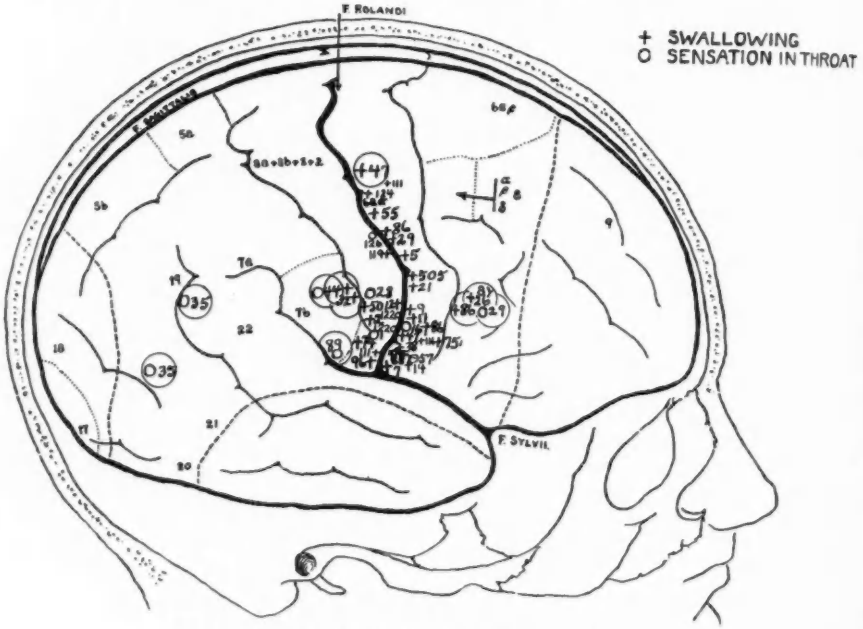


FIG. 10.—Swallowing and throat sensation.

(12) SWALLOWING AND THROAT SENSATION (fig. 10).

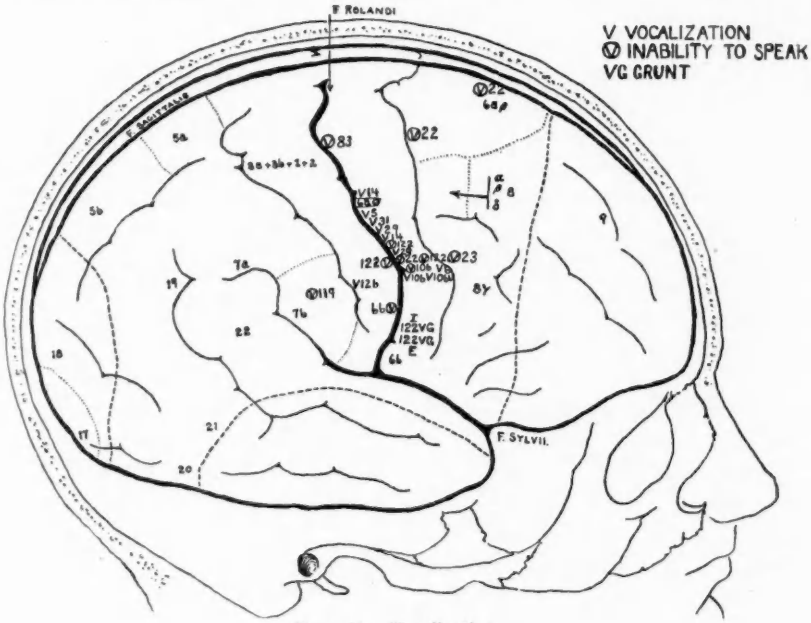
It has been necessary to exercise great care in the distinction of spontaneous swallowing from swallowing as a response to cortical stimulation. There were 32 examples of definite swallowing secondary to stimulation. Of these 23 were from precentral points. This means proportionally a much greater number of postcentral motor points than for face.

Throat sensation resulted from nine postcentral and four precentral points. Even when the grossly atypical location of the stimulation point of Case 35 is ruled out, these sensory points are spread over a much wider territory than are motor.

In Case 35 the response is doubtless displaced by a very large cyst posterior to these points from the margin of which epileptogenic discharge evidently took place. The patient described the sensation produced as "a feeling of filling up in the throat."

(13) Vocalization (fig. 11).

Six examples of vocalization included in this series were published by Penfield (1937) as the first example of such a response to stimulation



F IG. 11.—Vocalization.

of the cerebral cortex. We have been most interested in the rather sharply localized area for vocalization which is shown in this chart. In most cases, the response is obtained from a small area of a few millimetres in diameter. Once the area extended in a narrow band across the precentral convolution.

Vocalization may be produced by cortical stimulation in the precentral gyrus on either hemisphere. It was produced four times from the dominant and four times from the non-dominant hemisphere. It occurs without any associated motor phenomena. Its localization is between the area for eyelid movements above and mouth below.

The response may be illustrated by some of the findings in Case 14. This was the first example of vocalization encountered, and surprised the surgeon quite as much as the subject. Two discrete points were found near each other in this patient. The upper point in this patient was stimulated thirty-one times in succession and vocalization was the response each time. There was nothing to suggest the formation of words. The patient was unable to stop the cry or to influence it in any way, even when urged to do so. Stimulation at points a few millimetres distant gave no response. The second point lower down on the gyrus (V-14, fig. 11) gave vocalization, but at a definitely lower pitch. At the intensity used no movements could be elicited anywhere over the cortex. That is, the stimulation threshold was lower for vocalization than for anything else in this case.

In Case 122 it will be observed that inspiratory and expiratory sounds (122 VG, fig. 11) were produced from adjacent points. Both of these sounds, however, were grunts of short duration and were associated with sensation in the mouth. The expiratory grunt was repeated. These are not examples of true vocalization as found in the other cases. They resemble rather the grunt which has been reported by Foerster and others previously, but not the loud continuing cry of true vocalization.

In vocalization the sound continues if the stimulation continues until the patient's breath expires, when he may take a breath and cry again. Usually the vocalization is an expiratory vowel sound. The three points for 106 which are distributed across the precentral gyrus were adjacent to another point from which the sense of inability to speak was obtained. Only one vocalization point has been found on the postcentral gyrus.

The patient's subjective feeling of inability to speak, indicated by the letter " V " in a circle in fig. 11, has been elicited from a scattering of points which became more numerous near the vocalization region. These evidences of inhibition are not associated with convulsive discharge. Inability to speak was subjective as a rule. Patient 22, however, was told to count aloud and, while doing so, appropriate stimulation caused a definite hesitation, though it did not completely stop her. Afterwards she volunteered that it had been difficult to speak when she had been about half way through. Others have stopped counting, or have volunteered that they could not speak.

(14) Head Sensation.

No chart is made for this group. Out of the 11 responses called head sensation 6 were characterized as painful. Of these 6 responses, 3 were ipsilateral, 2 frontal and 1 not stated. It seems apparent, therefore, that all of these painful sensations are to be looked upon as evidences of referred pain from stimulation of the brain as an organ. This would seem to be contradictory to the statement made elsewhere by one of us (Penfield, 1934), that the brain is insensitive and pain within the skull is produced only by stimulation of dural sinuses, large dural arteries and deep in the fissure of Sylvius where the middle cerebral artery enters it.

In a case where stimulation of the hemisphere does produce pain or headache, the pain or headache comes from numerous points, showing that it is not a matter of cortical activation. Such pain is very rare, but it does exist. There were two other ipsilateral sensations in the general group which may also be considered as referred sensation.

This leaves only three contralateral head sensations which seem to be evidences of sensory head representation. To these may be added two contralateral neck sensations. All five of these points fall roughly into the general vicinity of the face area and are recorded in fig. 9 as H.

Head aura occurred eleven times. That is to say a head sensation was produced which was characteristic of the patient's habitual epileptic aura. This aura seemed to have no localized representation, but occurred from points spread widely over the hemisphere.

(15) Movement of Fingers (fig. 12).

Finger movements are among the best localized of the responses found in this study. Although the responsive points extend 5½ cm. along the length of the fissure of Rolando, very few are found more than 1 cm. distant from it.

Of the 102 recorded points, 77 are precentral and 25 are postcentral. The most common response was movement of all the fingers together. It seems likely that this may be looked upon as an individual movement, not a combination of separate movements with individual representation. This occurred from 45 precentral and 12 postcentral points. Flexion of the individual fingers followed 23 precentral and 4 postcentral stimulations. Extension was the response from 16 precentral and 4 postcentral. The other movements were twitches or were not described in detail. The thumb was next in frequency of response with 15 precentral points and 6 postcentral. The order of frequency of

individual fingers or combinations of fingers in this series is as follows: Index, 4 precentral and 1 postcentral; little, 4 precentral and 1 postcentral; ring and little, 2 precentral and 2 postcentral; index and middle, 2 precentral and 1 postcentral; middle, ring and little, 3 precentral; thumb and index finger and ring finger, 1 each precentral and postcentral.

It was interesting to note that the only grouped finger movements were of the thumb and index, the index and middle fingers, the ring

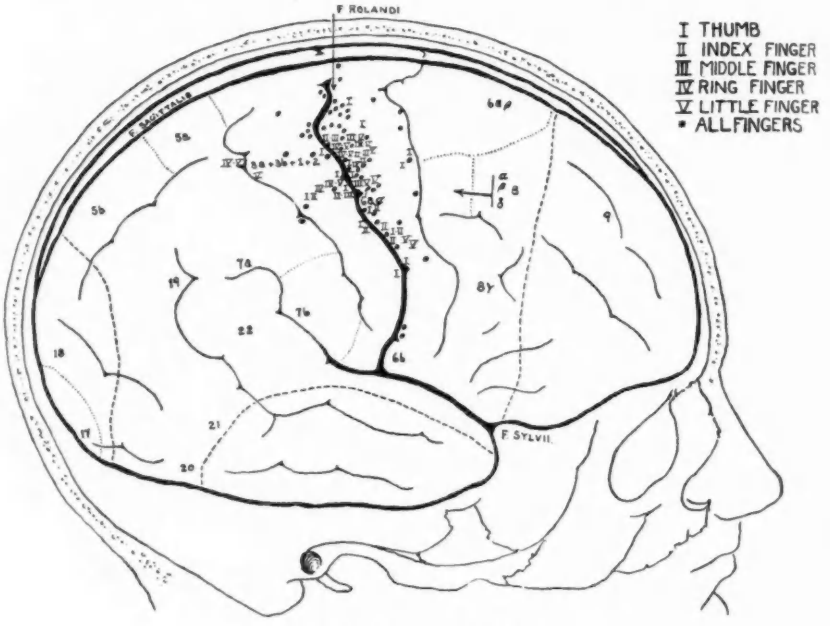


FIG. 12.—Movement of digits.

and little fingers, and the middle, ring and little fingers. We were surprised that the point for so useful and used a digit as the index finger was not encountered more frequently. It responded no more frequently than the little finger.

Flexion and extension responses were often separable in an individual case, and points for one digit were sometimes found separated rather widely as though these members had a comparatively large amount of cortex devoted to them. Patient 118 had some interesting finger responses. One point produced extension of the index finger together

with flexion of the thumb on the palm. Three other points responded with extension of all of the fingers and flexion of the thumb on the palm. But in this case an epileptogenic focal lesion lay near the finger area sensitizing it.

(16) Sensation in Fingers (fig. 13).

At first glance the striking feature on this chart is the comparatively small number of precentral points. Even so, they constitute over one-sixth of the total, for of the 158 points 130 lie behind the Rolandic

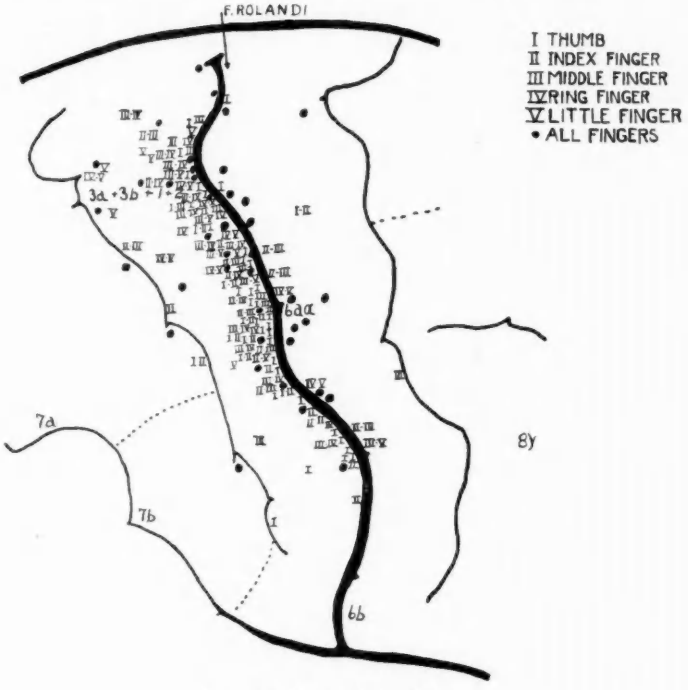


Fig. 13.—Sensation in digits.

fissure and 28 in front of it. They extend along the edge of that sulcus for about the same distance as the motor points, and are limited to a strip of surface cortex unusually narrow for sensory points when compared with the extensive spread already seen in previous sensory charts.

On forty occasions the patient felt sensation in all of the fingers. Twenty-seven of these points are postcentral and 13 precentral. In

forty instances there was thumb sensation, 34 from postcentral and 6 from precentral points. The remaining points are distributed as follows: index finger 13, index and thumb 10, index and middle 9, ring and little 9, middle and ring 12, little finger 7 and middle finger 5, ring finger 3, middle, ring and little finger 5, index, middle and ring finger 3, and thumb, index and middle finger 2.

We also have remarked that here, as well as in finger movement, multiple finger response has been seen only in consecutive digits. Painful sensation accompanied two of these stimulations, both points being postcentral. Sense of movement was present with 4 postcentral and 1 precentral stimulations.

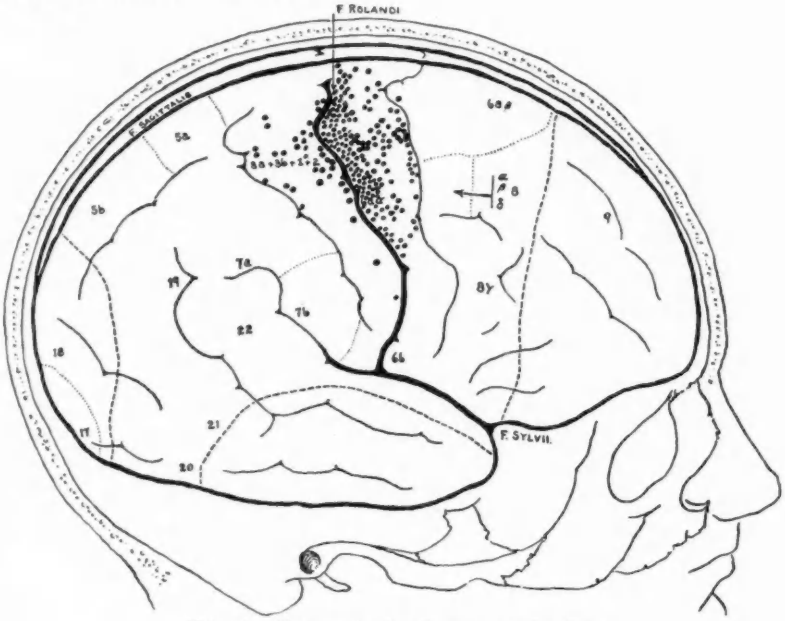


FIG. 14.—Movement of hand, arm and shoulder.

(17) MOVEMENT OF HAND, ARM AND SHOULDER (fig. 14).

From practically the same general cortical area as that from which we have already reported finger movements there appear those of hand, arm and shoulder. Two hundred and twenty-two of these responses appear and but thirty-six of them are postcentral. There is a curious subgrouping of responses between 1 and 2 cm. in front of the central fissure.

The joints represented in this chart are metacarpophalangeal, wrist, elbow and shoulder. Metacarpophalangeal joint movement has been described regularly as "movement of the hand" by persons reporting the objective responses at operation, and has been transferred to the charts as such. There are 71 precentral and 22 postcentral cortical motor points for hand movement. Forty stimulations produced flexion and 11 extension. The remaining movements were not further described.

In the arm proper 39 stimulations produced wrist movement, 67 gave movement of the elbow and 23 resulted in shoulder movement. Ulnar deviation of the wrist occurred once. Flexion was four times as frequent as was extension.

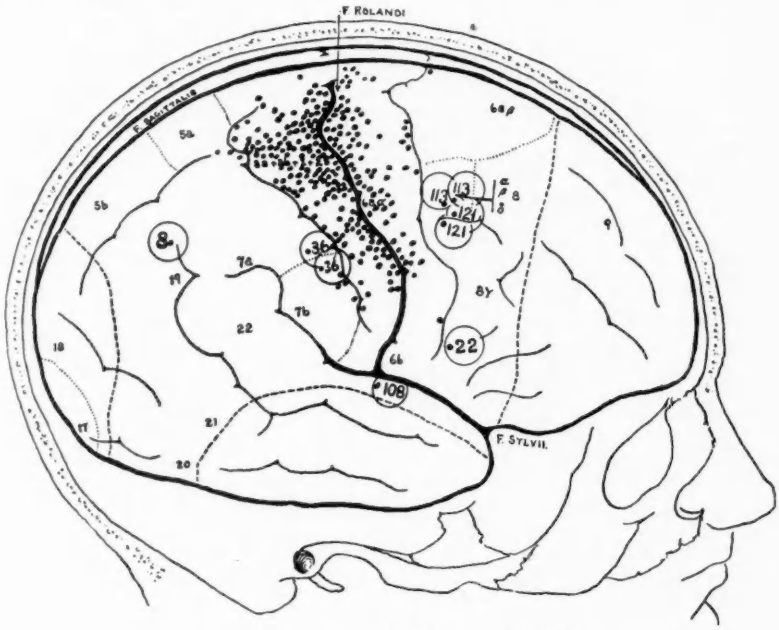


FIG. 15.—Sensation of hand, arm and shoulder.

It will be noted that the antero-posterior extent of motor response is not as great as that of sensation, recorded in the following paragraphs. The most distant motor points are 1½ and 2 cm. respectively from the Rolandic sulcus. The vertical distribution of points is for 5½ cm. along the central fissure.

(18) Sensation of Hand, Arm and Shoulder (fig. 15).

There are 279 points on this chart, 91 of these (32 per cent.) lie in front of the fissure of Rolando. Sensation in the hand was present during 36 precentral and 73 postcentral stimulations. No attempt has been made to differentiate between the back and the palm of the hand.

There are 170 points, stimulation of which has resulted in arm sensation. Fifty-five of these points lie in front of the central fissure. The response was localized in the wrist 5 times, in the forearm 20 times, in the elbow 4 times, in the shoulder 15 times. The remaining 126 points were called "arm" sensation. This term has not been exclusively confined to the region between elbow and shoulder.

Most of the sensations have been numbness or tingling. Pain has occurred twice. Sense of movement and desire to move were frequently located in this member. The sensations as such will be discussed later.

Of the atypical points on the chart point 108 on the temporal lobe was checked three times. The operative note made at the time states that it is "unexplained but must be accepted." Point 8 was not repeated but was quite definite. The patient had a tumour of the temporal lobe which may have displaced the cerebral tissue somewhat. In Case 36 an epileptogenic meningo-cerebral cicatrix lay just behind the sensory points indicated. Case 22 was that of a patient whose focus was near the midline in Area 6*a beta*. Points 113 and 121 are unusual only in their grouping together at a fairly distant point.

Attention is again called to the remarkable spread of sensory points anterior to and behind the central fissure.

(19) Movement of Trunk and Legs (fig. 16).

The voluntary muscles of the trunk and lower extremity respond only rarely. Doubtless more responses would have been obtained had it been feasible to stimulate the edge of the hemisphere and the mesial surface in the median longitudinal fissure more frequently. The danger of bleeding from sinus and tributary veins makes it unwise to stimulate here unless it is clearly necessary.

Twenty-six precentral points, two of which are on the mesial surface, produced these movements. Twenty-three of the points are for the lower extremity alone. The movements are quite equally divided among the different joints with the exception of the back, for which but one point was found. No motor points for individual toes were found.

In addition there are eight postcentral motor points. Neck move-

ments, but not head turning, are included in this chart, because the neck might be considered "trunk" from a functional standpoint. It is interesting, however, to note that neck movements (5 cases) are found in the vicinity of face movements at the lower end of the Rolandic cortex. This is the same area where certain rare trunk sensations grouped themselves in fig. 17.

The widely displaced points in Cases 62 and 111 are well removed from the epileptic focus of each which seemed to be high up in the

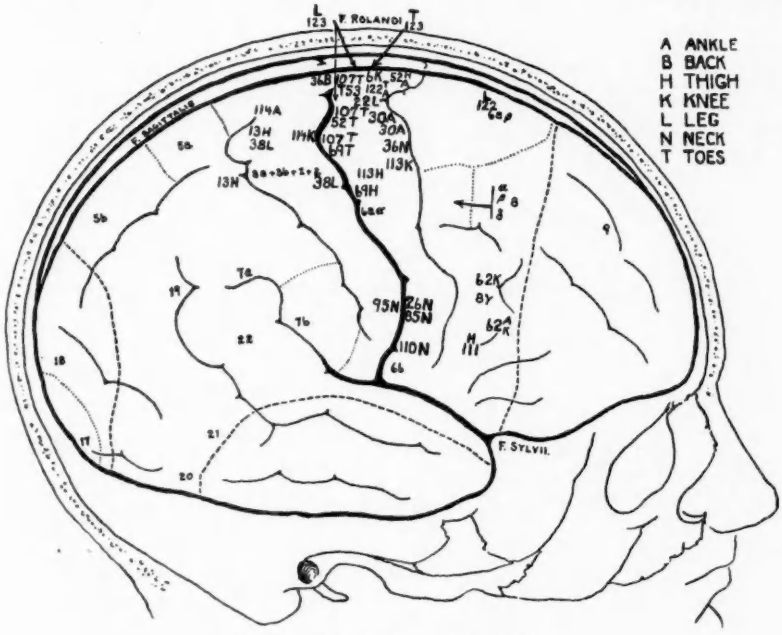


FIG. 16.—Movement of trunk and legs.

precentral region. Similarly in Cases 13 and 38 the patients were epileptics. In the first instance the focus was located at the very uppermost end of the central fissure. The lower end of the fissure was the firing point for the other.

(20) SENSATION IN THE TRUNK (fig. 17).

In the main group of response points there are eighteen postcentral and four precentral points. None were reported during stimulation within the longitudinal fissure. The response was often referred

accurately to a portion of the trunk which might extend from the opposite axilla to hip. In topographical sequence upon the cerebral cortex the trunk lies below thigh and hip and above shoulder. Epigastric auras in epilepsy will be discussed below but are not included here.

Curiously enough sensation was very rare in the lower sacral and genital regions. This fact may have resulted from the comparatively small number of stimulations within the central fissure, or possibly to a

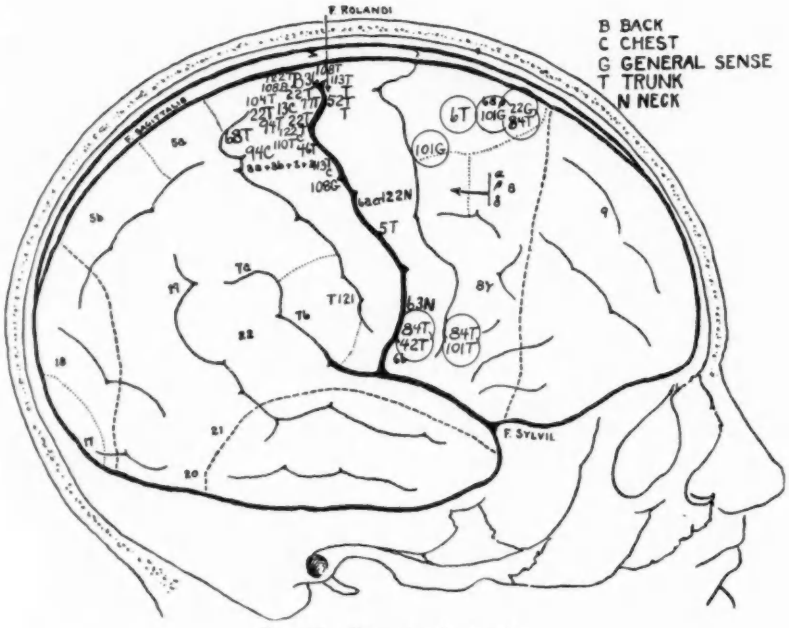


FIG. 17.—Sensation in trunk.

false sense of modesty. Sensation has been produced, however, in the contralateral side of the penis but no motor response. A second group of trunk sensation responses is to be found at the lower end of the fissure of Rolando. This recalls the fact that the neck and throat too are represented in this lower area where they lie adjacent to the face, and not above which would adjoin the principal trunk area.

Of this lower group Case 84 was that of a continuing post-epileptic hemiplegia in which sensory responses were present and more or less normally placed, but motor responses were lacking except mouth

movements. In none of these four cases was any trunk sensation elicitable in the principal trunk centre.

The responses from the lower centre were described as "pins and needles" in the contralateral side of the body, except for patient 84 who reported a sudden sense of being "paralysed in the right side." The sensation evidently spread through limbs as well as trunk.

A third group of responses were found to lie anteriorly in Field 6*a beta*. Response 6 produced a feeling of "flush" down the contralateral side of the body. This was repeated with the same result

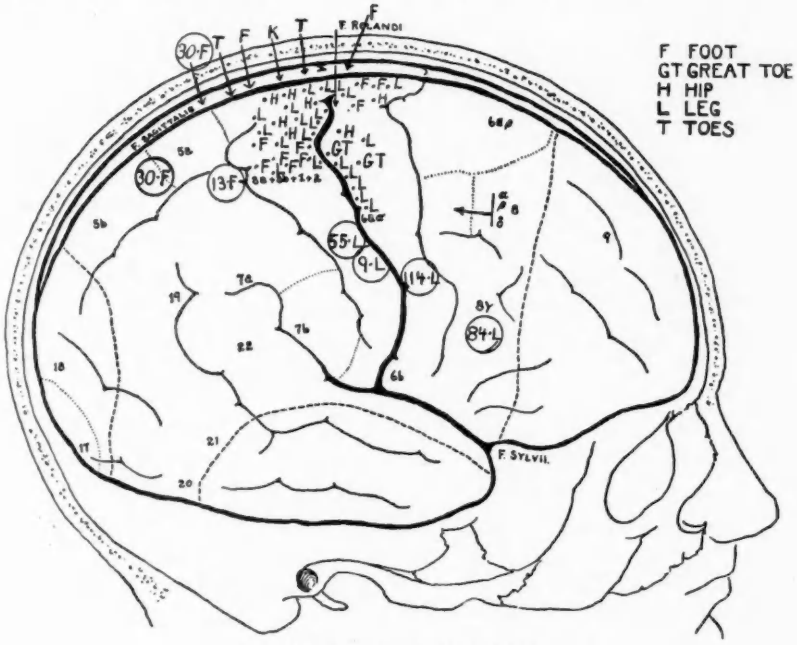


FIG. 18.—Sensation in leg and foot.

and there was no objective evidence of change of colour in the skin. The patient remarked after the second stimulation: "Sometimes I have that feeling before an attack." The responses 101 G were described as a feeling in the nerves all over and the epileptogenic focus seemed to be here. The sensation in that case was reproduced several times without warning.

The term "general sense" has been used in the chart (fig. 17) when the patient has been aware of some change in his body aside from an

epigastric aura but has been unable to localize it exactly. Thus one patient reported a feeling "as if something were moving inside." Three points in Area 6*a beta* and one point in the postcentral convolution elicited this response.

As far as our evidence from stimulation goes this Field 6*a beta* has more to do with bodily sensation than it has with the adversive movements which are discussed below.

(21) Sensation in the Leg and Foot (fig. 18).

Sensation is a more frequent response to stimulation than is movement in the lower extremities. There were 16 precentral and 33 postcentral sensory points, 1 precentral and 5 postcentral of which were on the mesial surface in the longitudinal fissure. In addition to tingling and numbness, sense of movement was reported once, desire to move once (114 H), and once a painful sensation. Sensation in the great toe alone accompanied two precentral stimulations. No ipsilateral sensation was described.

One point in Case 30 is seemingly far displaced but the responses were checked carefully. The other points separated from the main group are doubtless examples of epileptic effect, and Case 84 is that of the patient who was operated upon during post-epileptic hemiplegia.

(22) Adversive Turning of Head and Eyes (fig. 19).

By adversive movements is meant conjugate deviation of the eyes to the contralateral side and turning of the head to that side. Adversive movements of the eyes alone occurred as a large group of responses in an area which centres roughly in Areas 8 (*alpha, beta, delta*), but it extends back on to the precentral gyrus. It is remarkable that in spite of frequent stimulation the Area 6*a beta* above has not, in our experience, produced adversive movements of head and eyes as recently suggested.

Adversive movements of the head and eyes together occurred only in a few instances. These responses group themselves in the general area of face representation, as though head turning to the opposite side was allied to mouth pulling to that side. During operation the patient's head lies upon a soft ring and it is prevented from very much turning by the towels, but any attempt at turning is evident both to anæsthetist and surgeon. The more likely explanation of the difference between our results and those of Foerster is that we have probably used less

intensity of current and that we have eliminated from this study all true epileptic responses.

It is of interest that no downward deviation of the eyes was observed. This may, in part, be due to the fact that the patient's position under the tent makes it likely he would deviate his eyes down to see the observer spontaneously so that no change might be noted.

The deviation of the eyes to the opposite side from the lower point of Case 28 (fig. 19) was reported by the patient to be "towards a light"

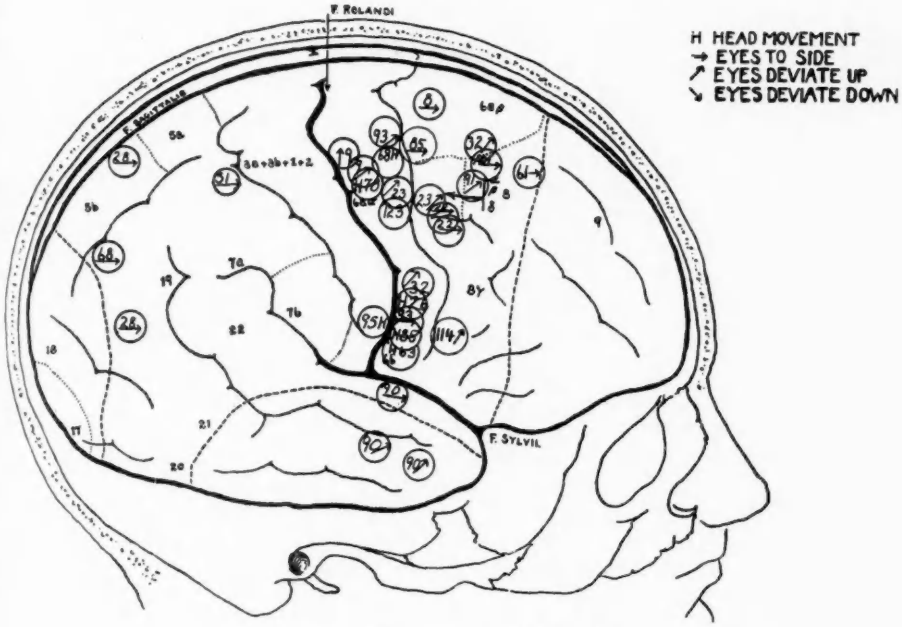


FIG. 19. — Adversive movements of head and eyes.

which he saw as a result of the stimulation. This is of interest in view of the ideas of some of the early investigators on adversive eye movements in animals. However, none other of the patients made a similar observation.

In Case 90 the unusual location of points for eye-turning led the surgeon to re-examine the responses with no warning before his stimulation, but the response was invariable. In two of the frontal responses the movement was towards the *ipsilateral side* instead of contralateral as in all the others. This might serve to explain

turning to the side of the lesion in focal epileptic fits which occurs as a rare exception to the almost universal turning of the head and eyes away from the discharging lesion. The frequency of head and eye-turning in such fits might lead one to expect it to appear more frequently than it has as a result of cortical stimulation.

The frequency of upward deviation of the eyes in epileptic seizures may perhaps be related to the frequency of upward deviation produced by frontal stimulation.

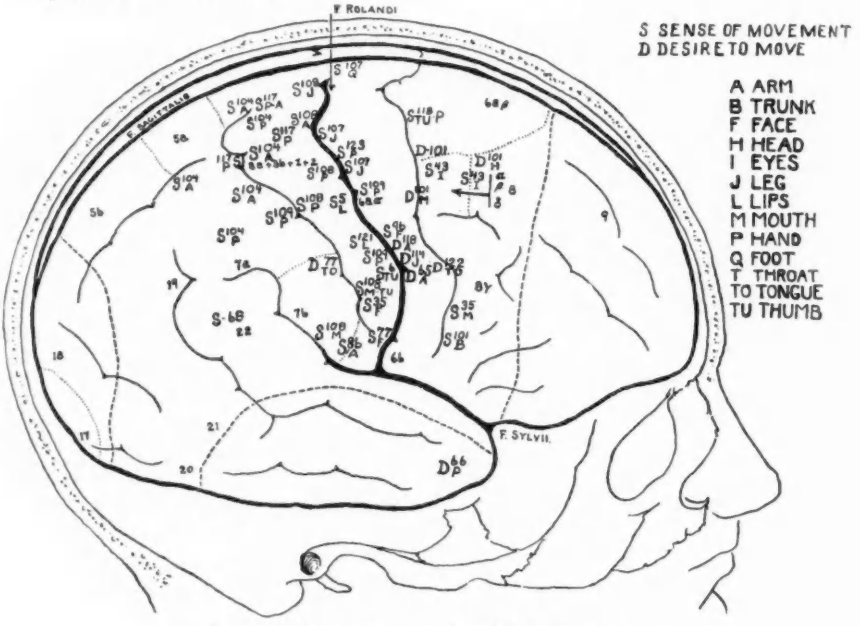


FIG. 20.—Sense of movement and desire to move.

In summary, therefore, there is evidence in this analysis only of a grouping of adversive head-turning responses in the lower Rolandic cortex and there is a larger grouping of conjugate eye deviation responses in the general location of the cytoarchitectural field 8 *alpha, beta, delta* called by the Vogts (1926) the most easily stimulable area for eye movements as the result of their work upon the ringtailed monkey (Meerkatze).

(23) SENSE OF MOVEMENT AND DESIRE TO MOVE (fig. 20).

The sensation of movement in a part was reported by Cushing. We have been somewhat surprised at the frequency of this sensation

as it has proved to be the third most frequent description, coming thus after numbness and tingling. The patient realized he had not moved but observed that it felt as though his finger, arm, foot, &c., had moved. When the point (S118 TU P, fig. 20) was stimulated the patient said, "Look at my thumb; it feels as though it were twitching. That's the warning I get." He referred to his habitual aura. There was no observable movement of the thumb.

This response has occurred fifteen times anterior to the fissure of Rolando and twenty-seven times posterior to it. In general the points fall within the same zones as other forms of sensation (*see* S, in fig. 20), the face lying below and upper and lower extremities above.

The response of desire-to-move is also a definite experience to the patient and, like all other unexpected responses, was usually verified by re-stimulation without warning to the patient. These responses were all in front of the central sulcus except D77, which was a desire to move the tongue. The patient said the tongue did not actually move, but as the mouth was closed this could not be verified objectively. D66 lay upon the temporal lobe in the case of an intelligent young woman who observed that she wanted to move her opposite hand up and down. It was associated with a slight sensation in the abdomen. This abdominal sensation was similar to her habitual epileptic aura and a typical attack was produced by stronger temporal lobe stimulation later on. Nevertheless, as the desire to move the hand was again produced at an adjacent point and could not be produced from stimulation elsewhere, it is included here.

The tendency to localization of the desire-to-move anterior to the precental gyrus is interesting, as it seems to relate this desire for movement to motor rather than to sensory function.

(24) Ipsilateral and Bilateral Responses.

There were no examples of verified isolated ipsilateral sensation. This is true even for face and tongue.

There were no motor responses of the ipsilateral extremities and none of the face, except where the movement was part of a bilateral grimace. There was one exception to this last statement, and that was in the case of a little girl who had a focal traumatic lesion just anterior to the Rolandic face area. This produced marked epileptic spread of response and an ipsilateral face movement that was verified repeatedly.

Bilateral motor responses in the extremities are also completely

lacking. Bilateral sensation has occurred only rarely, as mentioned above, when a sudden generalized feeling throughout the whole body was produced from Area 6*a beta* (101, fig. 17). Bilateral sensations do occur in the face and in the tongue and bilateral movement in the face, tongue and jaw. Three times patients have reported sensation in both eyes. Once the description was "both eyes like paralysed." The other two had a sensation of lifting the eyes when the eyes did not actually move.

(25) Autonomic Responses.

Pupillary change could not always be watched for. In one case both contraction and dilatation of the pupil was produced at different points by frontal lobe stimulation. Alteration in pulse was observed only once when stimulation of the right frontal pole caused the pulse-rate to double. Repetition of this stimulation, however, caused only a quickening for a few beats.

We have found no valid evidence of a vasomotor centre on the convexity of the cerebral cortex. Once the face flushed as the result of stimulating in the postcentral face area, but it may have been a manifestation of an epileptiform discharge. Perspiration seems to have occurred once as a result of low precentral stimulation.

Salivation occurred in two instances, both from the lower postcentral region, and it accompanied tingling in the tongue once and swallowing the other time.

There is no evidence of gastro-intestinal response to stimulation of the cortex. But in four patients a sensation of nausea was produced. Patient 29 felt nauseated while precentral stimulation was causing vocalization. The other three all had nausea produced by stimulation of the parietal lobe. In each instance it was a familiar aura of an attack. In Case 15 stimulation at two points along the margin of a parietal lobe cyst produced nausea and a little later, when the patient wakened from a natural sleep, he was found to have had a bowel movement. Little importance should be attached to this, however. Vomiting has occurred in one case and was probably incidental.

Epigastric aura.—Sensation in the epigastrium is so frequently an epileptic aura that it was searched for carefully, but was elicited only three times as an aura. In all three cases the localization was in the posterior-superior parietal lobe just behind the postcentral convolution. One patient (Case 24) called it a feeling in the chest, one (Case 94) a rising feeling in the chest and one (Case 20) a

weakness in the abdomen. So far as this meagre evidence goes, therefore, the epigastric aura has a localization in the superior parietal lobe posterior to the Rolandic area.

Emotional disturbance.—Weeping has occurred suddenly in two cases only and in both instances the stimulation was high precentral. Laughing occurred only once (Case 110—*see* report above) and then resulted from postcentral stimulation which gave sensation in the lower lip and it was not repeated. It may be said that stimulation of the cortex gives rise to an emotional sensation only very rarely. In fact, there was only one repeated and verified response and in this case weeping was habitual at the onset of a convulsive seizure.

(26) Discussion of Illustrative Cases.

A number of factors must be considered before these results are compared with data from animal experimentation and anatomical charts. It must be remembered that although we have transferred our results to a standard human chart on which are marked cytoarchitectural fields we do not know what the architectural pattern is in any particular case and how much these boundaries may vary from individual to individual. We have only measured roughly from the central fissure and from the fissure of Sylvius and the sagittal fissure. No greater accuracy can be achieved in any stimulation study.

It has been our routine procedure to begin with the lowest effective stimulation strength and to work up gradually. The central fissure is always outlined by stimulating up and down both sides but sometimes sufficient time was not available for complete mapping. Sometimes the Rolandic cortex proved to be refractory to stimulation except at a few points. The reader may get a truer perception of the meaning of our figures by reviewing the following electrical explorations.

Case 6.—F. W., a boy, intelligent and co-operative, suffering from focal epileptic seizures characterized by a sudden feeling in the right side of body and movements of right hand. Left osteoplastic craniotomy was carried out and excision of a small area of abnormal indurated cortex anterior to precentral gyrus.

Referring to figs. 21 and 22 the results from above down on the postcentral gyrus were:—

14. Tingling from the knee down to the right foot, no numbness.
13. Numbness all down the right leg, did not include the foot.
12. Numbness over the wrist, lower border, right side.
11. Numbness in the right shoulder.

3. Numb feeling in hand and forearm up to just above the forearm.
10. Tingling feeling in the fifth or little finger.
9. Tingling in first three fingers.
4. Felt like a shock and numbness in all four fingers but not in the thumb.
8. Felt sensation of movement in the thumb; no evidence of movement could be seen.
7. Same as 8.
5. Numbness in the right side of the tongue.

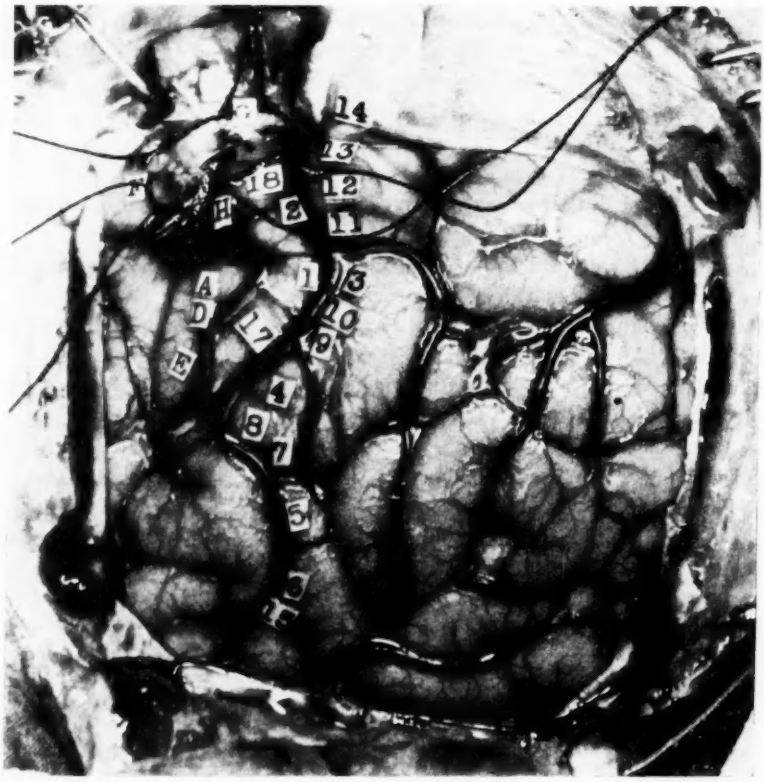


FIG. 21.—Cerebral cortex of Case 6, as photographed at operation. The tickets of reference indicate responses which are described in the text. *See also* fig. 22.

6. Tingling feeling in the right side of the tongue, more at the tip.
15. Tingling in the tongue, associated with up and down vibratory movements.
16. Numbness, back of tongue, mid-line.

Precentral gyrus from above down:—

(G) Flexion of knee.

18. Slight twitching of arm and hand like a shock, and felt as if he wanted to move them.

2. Shrugged shoulders upwards; did not feel like an attack.

(H) Clonic movement of right arm, shoulders, forearm, no movement in trunk.

(A) Extreme flexion of wrist, elbow and hand.

(D) Closure of hand and flexion of his wrist, like an attack.

17. Felt as if he were going to have an attack, flexion of arms and forearms, extension of wrist.

(E) Slight closure of hand; stimulation followed by local flushing of brain; this was repeated with the strength at 24. Flushing was followed by pallor for a few seconds.

(B) Patient states that he could not help closing his right eye but he actually closed both (fig. 22).

(C) Made a little noise; vocalization. This was repeated twice. Patient says he could not help it. It was associated with movement of the upper and lower lips, equal on the two sides (fig. 22).

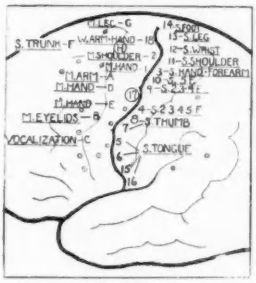


FIG. 22.

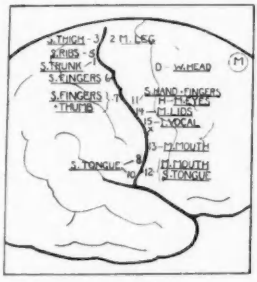


FIG. 23.

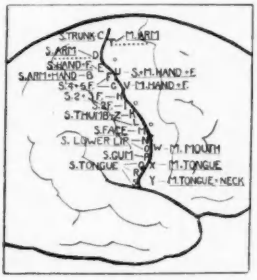


FIG. 24.

FIG. 22.—Chart of cortical stimulation of Case 6, as prepared at the time of operation. The points are the same as in fig. 21.

FIG. 23.—Chart of cortical stimulation of Case 22, as prepared at operation. The figures and letters indicate localization of points referred to in the text.

FIG. 24.—Chart of cortical stimulation of Case 110, as prepared at operation. The points correspond to those in fig. 4 and the responses are described in the text.

Below C and 17 on the precentral gyrus no responses were obtained even with a strong stimulation, although small attacks had been produced at 17 with a weak stimulus and at H with a stronger one. This refractory condition may be transient but is often encountered at various areas in these cases.

This case illustrated several peculiarities mentioned above, i.e. the desire to move the arm and hand at 18 whereas all other sensory responses were postcentral. The curious sensation as of flushing in the

opposite side of the trunk was an aura of his attack and yet sometimes similar sensation has been secured from this area in other cases.

Case 22.—H. T., a woman aged 20, suffering from focal epilepsy originating apparently in the right frontal lobe near 6*a beta*, characterized by: an aura in which "the surroundings seem a little queer" and her thoughts turn to past events. This is followed by loss of consciousness, tonic rotation of eyes and head to the left, twitching of the left face, clonic convulsive movement of left arm and leg, tongue biting and incontinence, in the order given.

Stimulation from above down on the postcentral gyrus with thyratron (bipolar) at 26 gave (fig. 23):—

3. Feeling in leg, "numb," hip to knee left side.
5. Prickly feeling left side of trunk at lower margin of ribs.
1. Numbness left side of body from axilla to crest of hip.
6. Tingling all fingers except thumb.
7. Feeling in all fingers including thumb (no movement).
8. Numb feeling left side of tongue near tip.
10. Same as 8.

On the precentral gyrus:—

2. Tonic movement, left leg, no sensation, "leg moved itself."
11. Tingling left hand and fingers, no movement.
14. Marked closure of both eyes; deviation of left eye to side of stimulation. Other eye not seen.
15. Patient said she was unable to speak and unable to open eyes. No movement.
(X) Convulsive attack not like her habitual ones. It was characterized by clonic movements of mouth, left eye and left face with vocalization.
13. Mouth drawn markedly to left, no feeling in tongue near tip.
12. Mouth drawn to left and feeling left side of tongue near tip.
(D) Peculiar feeling in head; unable to talk for several seconds. Felt as though she wanted to turn her head to the left. No eye movements.
(H) and (G) Eyes deviated markedly upward and to left.
(M) Several small attacks produced from this point and its vicinity during one of which eyes went to left and downward. Once head went to left and once, after stimulation at depth of 2 cm. in brain, the eyes went sharply to left and upwards followed by sharp turning of head to left. Once stimulation near M caused her to say, "felt very peculiar, everything far away, a little bit like before the attacks occur." Sensation in face and lip was elicited but the markers were washed away.

This case illustrates certain points of interest. Sensation in hands and fingers was elicited from the anterior lip of the fissure of Sylvius at 11. At 15 there was inability both to speak and to open eyes. At

D she did not use the word "speak," but said she could not talk. At 12 the same stimulation produced movement of mouth and sensation in the tongue, which means that that point will appear twice on our summary charts, once for each response.

Adversive movements of the eyes were obtained easily at H and G, but no head-turning was obtained until small epileptic seizures were produced. The desire to turn the head was obtained at D and with it a sensation in the head and inability to talk. She used the word "speak" for 15 as mentioned above.

If figs. 22 and 23 are compared the sequence is seen to be the same, but some responses that might be expected are absent in each. No sensory response referred to the trunk was obtained in one, none to the leg in the other, to the face in one or to the throat in either. As is often the case less detail is elicitable from the precentral gyrus. In fig. 22 vocalization is obtained but no response in the lower face or tongue. In fig. 23 vocalization is lacking but mouth and tongue are present.

This variability probably depends upon pre-existing conditions which are not always the same, for we have found, in those cases that were opened up a second time, that different responses were elicitable. The pattern of responses may depend also upon which spots are first stimulated on the day of operation. But the existence of grossly atypical and distant responses argues that in these cases there is a very important role played by abnormal lesions and particularly by the epileptic habit.

(27) Summary of Localization.

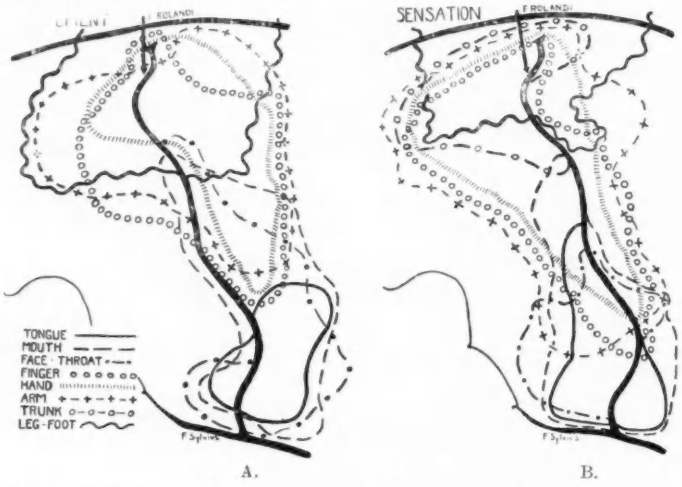
During any one exploration the responses of the sensorimotor cortex vary little, if at all. After stimulation has been carried up and down both sides of the fissure of Rolando and tickets placed upon each positive response, as in fig. 4, the whole process may be repeated with the same intensity of stimulation and the result will usually be identical. The same areas will give no response and the positive points will repeat themselves. But if the same hemisphere be explored at a later operation after a lapse of time, as we have done in five cases, the result may be quite different because areas quite active at the first operation may be mute at the second, and areas which gave no response may later be easily activated.

If a point on the precentral gyrus two-thirds of the distance from the longitudinal fissure to the fissure of Sylvius be stimulated in six different individuals the result will vary greatly so that any standardized

chart which localizes the position of those points upon the cortex may be correct for one individual (e.g. figs. 22, 23 and 24) but not for all.

Superimposing all the points of individual cortical charts results in the diagram drawn up in fig. 25. The outlines of finger localization correspond to that of arm and yet in any individual chart (*cf.* figs. 22 and 23) arm will be found above fingers.

As may be seen by reference to this figure (fig. 25) movement has a proportionally larger representation anterior to the central fissure and sensation a larger representation posteriorly, and the two areas, motor and sensory, overlap each other consistently and correspond to each other horizontally.



A. B.

Fig. 25.—Summary of sensory and motor findings in figs. 5 to 20. The lines enclose the areas within which responses were obtained for each subdivision of the body. A. movement. B. sensation.

But in spite of this variability of geographical location illustrated in fig. 25, the sequence of motor and sensory representation from above down is almost invariable. We have expressed the motor sequence in summary form in fig. 26. The list from "toes" above down to "swallow" at the bottom indicates that our conclusions in regard to this sequence is that of the general consensus of opinion with a few additions. The horizontal bar opposite each name indicates proportionally by its length the total number of such responses obtained. The length of the bar to the right of the vertical line shows the number of precentral responses and the length to the left the number

of postcentral responses. This illustrates that the hand has responded most frequently, lips next, followed by elbow, wrist, jaw, swallowing and thumb, etc.

Fig. 27 is made up in the same manner for sensory sequence, and here again the hand leads in total number of responses. Tongue now is second in numerical sequence with lips, arm, jaw, face, thumb, and leg following after. Hand and arm sensation have a comparatively large number of precentral responses as well as face and leg, whereas fingers and thumb have relatively few precentral responses.

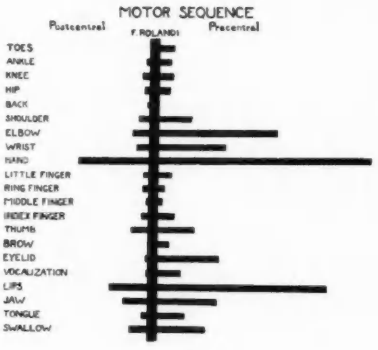


Fig. 26.

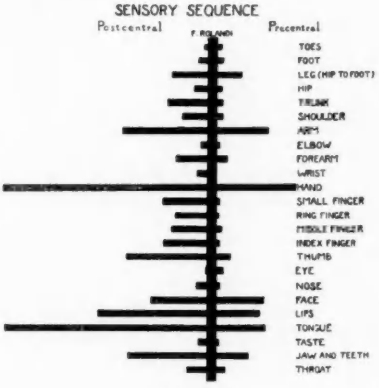


Fig. 27.

Fig. 26.—Motor sequence chart for right hemisphere. The list from "toes" to "swallow" indicates the sequence of motor responses in the Rolandic cortex from the median fissure above to the Sylvian fissure below. The broad vertical line represents the fissure of Rolando. The length of the individual horizontal lines to the right indicates the proportional number of points anterior to central fissure. Their length to the left indicates the number of points posterior to that fissure which gave responses in the part as shown by the names in the column to the left. All face movements are included under the heading of "lips" on this chart. Neck movements have been omitted because of the inconclusive localizing value of the small number of points found. Hand movements in this chart include movements of all of the fingers together.

Fig. 27.—Sensory sequence chart prepared as in fig. 26. Contrary to movement, face sensation is separated from lips. Head sensations have been too scattered to justify their inclusion, and neck sensation points are too few in number.

The sequence relationships may be considered from another point of view illustrated by the homunculus in fig. 28. In figs. 26 and 27 it is seen that toes begin at the top and the members follow in order as though representing a man hung upside down, but that thumb is followed by the head as though the head and neck were erect and not inverted. The larynx represents vocalization, and pharynx swallowing and throat sensation.

The homunculus gives a visual image of the size and sequence of

cortical areas, for the size of the parts of this grotesque creature were determined not so much by the number of responses (as for figs. 26 and 27) but by the apparent perpendicular extent of representation of each part when these responses were multiple for the same part.

The large size of the thumb and lips indicates that the vertical extent of Rolandic cortex devoted to those parts in individual cases is very large. Thus the trunk is quite small and the legs and head

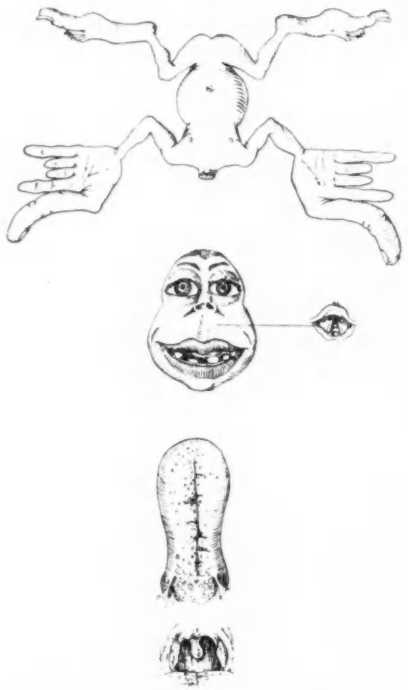


FIG. 28.—Sensory and motor homunculus. This was prepared as a visualization of the order and comparative size of the parts of the body as they appear from above down upon the Rolandic cortex. The larynx represents vocalisation, the pharynx swallowing. The comparatively large size of thumb, lips and tongue indicate that these members occupy comparatively long vertical segments of the Rolandic cortex as shown by measurements in individual cases. Sensation in genitalia and rectum lie above and posterior to the lower extremity but are not figured.

exceedingly small, while the tongue, which usually occupies a comparatively long strip of the Rolandic lip, is large. The homunculus may be said to be both motor and sensory as the sequence pattern is roughly the same, although there are differences. Comparison of figs.

26 and 27 shows that eyelids have a large motor representation. Sensation in the eyes is usually of movement. Eye-turning is not included in the chart. It will be noted, too, that neck is above lips in both sequence charts. The number of responses is as yet too small to be finally certain of the sequence position of neck, of taste and of nose. Foerster places neck between thumb and upper face for both sensation and movement. He likewise places jaw below tongue for both, whereas we would place sensation in teeth and gums below tongue but jaw movement above. Aside from these observations the homunculus represents true sequence. Presumably rectum and genitalia should be placed above feet, that is within the longitudinal fissure, but our evidence is not sufficient for conclusion and they seem to be somewhat posterior to feet.

(28) Quality of Cortical Sensation.

The quality of sensation resulting from cortical stimulation is of interest. In 369 responses the quality was not stated simply because it was the same as in the first or second stimulus which was recorded. In 204 responses it was called tingling or electricity, 131 times numbness, which at times was explained to mean numbness with tingling, at other times absence of all sensation. In 49 responses the patient had a sense of movement when no objective change of position occurred. This applied to a sense of movement of both eyes to sense of movement in one arm, one finger, &c.

There is no localization of quality of sensation, either pre- or postcentral. Eleven times the patient reported a sense of pain in one extremity or peripheral part; it was never severe. Thirteen times a feeling of cold was reported. This last sensation was most frequently applied to the face. As the sense of heat was only mentioned twice it seems possible that tingling was taken for a sense of coldness. A sense of blood rushing was felt ten times. Thickness was the description five times and each time applied to the tongue; swelling once and this also to the tongue.

Desire-to-move, as indicated in fig. 20, has been a definitely reported experience. It is not clear that this is a sensation, but as it was verified by repeated stimulation without resultant movement it becomes an interesting phenomenon, especially as it was anterior to the central fissure in all but one instance. This is to be contrasted with the sense of movement which is chiefly postcentral in location. A feeling of inability to carry out some movement has also been described as

though the patient were made aware of stimulation of an inhibitory mechanism. This has most often been described as inability to speak.

(29) Cause of Atypical Responses.

Gross lesions of the brain which deform the hemisphere and displace or alter the Rolandic portion of the brain cause displacement or obliteration of representation. This may explain some of the unexpected results in this report. The lack of anæsthesia doubtless accounts for many differences between human and experimental results, as practically all experimental investigations have been carried out under light ether or barbiturate anæsthesia which gravely alters the reactive state of the cortex. Further, however, it may well be that the human cortex has normally wider associative connections more easily activated.

But what is the significance of a response to electrical stimulation of the cortex? When a motor response is thus produced it is evident that a chain of neurones is activated and an effective impulse passes out to the periphery. When cortical stimulation produces a sensation the mechanism is not at all obvious. It may be that a neurone chain has been activated. If so, whither is the impulse carried? It seems likely that normally the sensory circuit in question is activated by a peripheral stimulus, the resultant impulse of which rises in the central nervous system to a point as high as the postcentral convolution.

Does it stop there or is that point only a way-station on the road to a higher level? It is quite possible that sometimes the stimulation may affect the further course of that sensory pathway toward a higher physiological level. It is also possible and probable that for both motor and sensory responses distant stimulation may activate the primary motor and sensory areas through a connecting neurone chain. These connections are doubtlessly established by pre-existing and sometimes transient conditions.

Sherrington has pointed out the instability of a cortical point. In Case 110 (figs. 4 and 24) above we have shown that a motor response may be moved from the posterior lip of the precentral gyrus to the anterior lip and a sensory response from the anterior lip of the posterior gyrus across that gyrus to its posterior lip by the activating effect of rhythmic repeated advancing stimulation. We have made the same observation in several other cases.

But widespread displacement or extension of function from its usual localization is in these cases most often due to the local or diffuse effect of a lesion which is giving rise to epileptiform seizures, or to the fact that

epileptic discharges habitually take place in the cortex even though no objective lesion can be found.

It seems evident that this process may: (*a*) Sensitize or activate areas of cortex; (*b*) may cause widespread displacement of response, and perhaps (*c*) under other circumstances, render normally excitable areas inexcitable to the electrode.

(*a*) *Epileptic activation.*—The epileptic process may sensitize a part of the cortex so that evidence of the nature of neural activity inherent in that part may become evident, although under normal conditions no response to stimulation would be expected.

This applies especially to the parietal and temporal lobes where visual phenomena and even memory processes may be elicited as reported by Penfield (1937). Under such circumstances the repeated epileptic discharge seems to have established a sort of conditioned reflex. A similar effect is seen upon the sensori-motor cortex about the Rolandic fissure in certain cases where an oft-repeated seizure has produced a Jacksonian march. As a result the parts of the Rolandic cortex involved in the habitual march may give a more detailed and finely divided response to electrical stimulation than usual. This we have called epileptic activation.

(*b*) *Spread.*—For example, if an epileptogenic focus be located at some distance from the Rolandic cortex at the level of the arm area stimulation of the arm area gives, as expected, a sudden feeling in the arm. But stimulation of the cortex about the focus and over the intervening cortex produces likewise the same identical sensation in the arm. It is apparent that the whole large area in question has developed the capacity of discharging selectively that one Rolandic response.

This is an evident spread of response due to the influence of an epileptic focus. In a so-called idiopathic case of epilepsy where no objective focus can be demonstrated the same spread may occur.

(*c*) *Inhibition* of response evidently obtains in the cerebral cortex of epileptic patients. It seems likely that in some cases this is due to post-convulsive vascular changes (Penfield, 1933). In others there may be a true post-seizure refractory stage.

(30) Discussion.

After the elimination of instances of widely displaced responses due to epileptic spread and to pathological distortion there remain the great majority of responses to be considered as evidence of localization of

function. These are normal responses to be expected from the human cerebral cortex free from any anæsthetic effect.

We find no evidence in favour of the extension of the motor cortex to Areas 6*a* *beta*, 5 and 22 as described by Foerster (1936A) and illustrated in fig. 3. Somatic motor responses are obtained from the Rolandic cortex, i.e. pre- and postcentral gyrus, but not from other areas of cortex if subconvulsant stimulation be used. Even turning of the head and neck to the opposite side (adversive movement) is not obtained under normal conditions outside of the Rolandic cortex. From the animal experiments of the Vogts we had expected that in man stimulation of Area 6*a* *beta* would produce head aversion, but so far in our experience and with the technique which we have employed, Area 6*a* *beta* has not proved to be a "frontal adversive field."

The difference between our conclusions in this regard and those of Foerster may be only a difference of interpretation explained as follows: We have used a minimal intensity of stimulation in the Rolandic zone and have then increased it markedly and even altered its wave frequency to try to produce results in the more distant cortex. But we have not included epileptiform seizures among our responses. On the contrary we have eliminated all convulsive movements, whether tonic or clonic. The criterion of an epileptiform seizure is that the phenomena produced by stimulation continue and may advance after withdrawal of the electrode.

There is great similarity in the mass movements or turning movements which Foerster obtained from the different "extra pyramidal" cortical areas outside the Rolandic cortex, and it seems likely that use of strong faradic currents made it possible to obtain them and that they are in reality evidence of an epileptiform discharge. Adversive movements occur so frequently during such discharges, in various localities as soon as the discharge involves any considerable part of the hemisphere, that it seems probable the mechanism of its production is brought into play by the fit without its being a manifestation of localized cortical function.

As a simple motor response adversive head-turning is produced occasionally from the lower end of the precentral gyrus, while conjugate contralateral deviation of the eyes may be produced by stimulation in the vicinity of Area 8 *alpha*, *beta*, *delta* in and just anterior to the precentral gyrus.

Our results indicate that stimulation of the precentral gyrus in a zone next the central fissure most frequently gives rise to motor move-

ments (fig. 29). But with no increase in stimulation strength there are in numerous cases responses from points anywhere over the precentral gyrus. From the postcentral gyrus also, but much less frequently, motor responses may be obtained, especially its anterior lip as shown in fig. 29.

Thus our results from stimulation resemble those of Grünbaum and Sherrington in the chimpanzee except that they got no responses from the postcentral gyrus (*cf.* figs. 1 and 29). This may be due to a

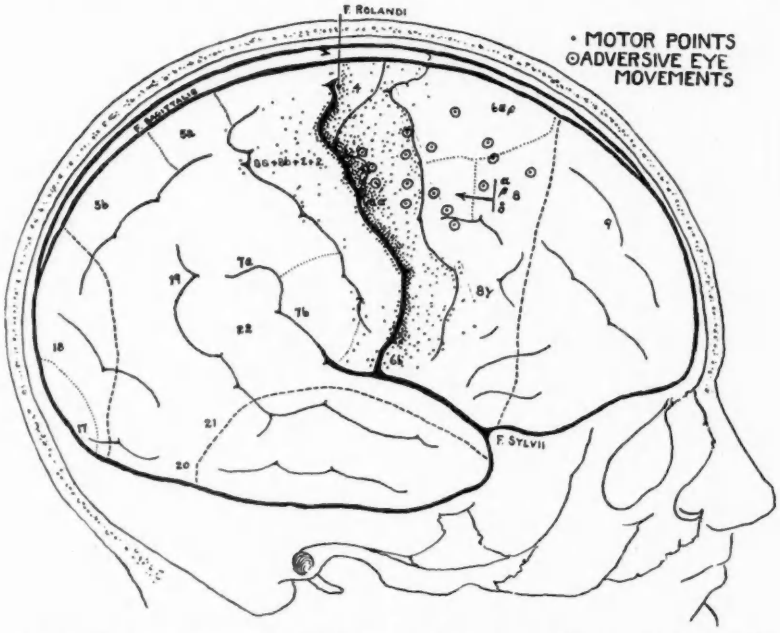


FIG. 29.—Motor cortex. Each black dot represents an actual motor response. The number 4 indicates where Area 4 extends from the anterior wall of the fissure on to the surface, according to Vogt. The remainder of the outer surface of the precentral gyrus is made up of Area 6*a alpha*. ⊙ = conjugate movements of eyes to the opposite side or upward.

difference in man and anthropoid, or more likely it is due to the light anæsthesia which it was necessary for them to use during the stimulation. If in fig. 1 the cytoarchitectural map of Bucy below be compared with the stimulation map of Grünbaum and Sherrington above it is evident that the motor responses occurred in both 4 and 6 with no particular tendency to follow the cytoarchitectural pattern, except to cover about the same extent anterior to the central fissure. In the

same way in fig. 29, where every dot indicates a response, it is shown that close proximity to the fissure on the precentral gyrus renders response most likely without any particular change in those regions where Area 4 spreads out on the surface.

As Area 4 occupies the whole anterior wall of the central fissure this is no doubt the part activated, but Area *6a alpha* on the precentral gyrus obviously contains neuronal connections with 4, which may often be activated by a minimal stimulus. Such secondary connections must

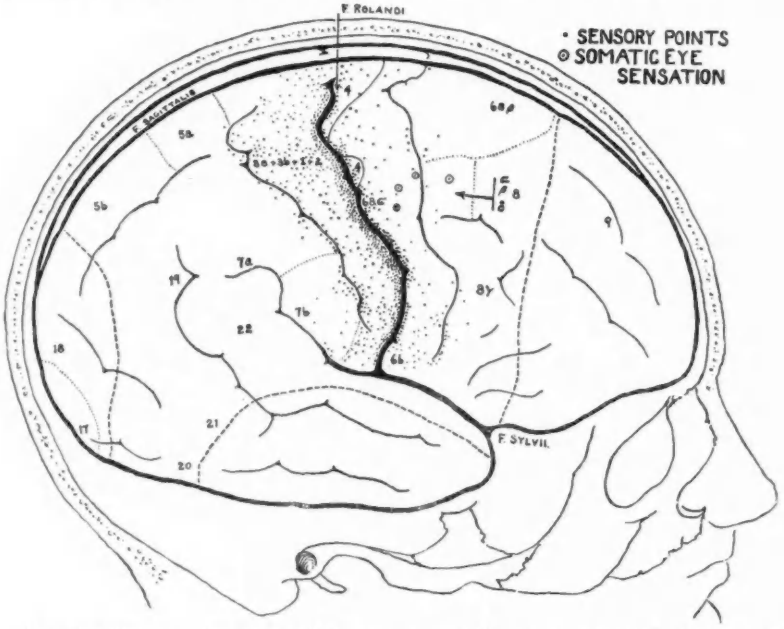


FIG. 30—Sensory cortex. Black dots represent actual sensory responses in some part of the body. ⊙ = sensation in the eyes.

also be possible from the postcentral convolution, especially for movements of hand, arm and shoulder (fig. 14), although these connections are less numerous or less stimulable.

Including these secondary areas the motor cortex, in the broadest sense, should be said to include precentral and postcentral convolutions; that is Areas 4, *6a alpha*, 3, 1 and 2. But Area 8 *alpha beta delta* probably should be added, as conjugate deviation of the eyes seems to extend forward over this general region as shown by the dotted circles in fig. 29.

Similarly, cortical representation of somatic sensation is found in the postcentral convolution and most often in its anterior lip. But it is also found in Areas 4 and 6*a alpha* of the precentral gyrus (fig. 30). Here again it is impossible to tell from stimulation results whether the responses are obtained primarily at one point and secondarily at another. The fact is that the responses were obtained by the same strength of stimulus, usually minimal. The extension of sensation over the precentral gyrus is more frequent than of motor responses over the postcentral gyrus (*cf.* figs. 29 and 30).

These results are in perfect accord with the anatomical work of Poliak (1932) who predicted that sensory representation would prove to be both pre- and postcentral. It also conforms to the theories of Dusser de Barenne (1935, 1936) based upon strychninization of the cerebral cortex. His work suggests clearly that both pre- and postcentral gyri are normally involved in some way in the elaboration of cortical sensation.

It is not infrequent that stimulation produces sensation and movement both in the same part, but never sensation in one and movement in another. So far as our own results go, therefore, it seems appropriate to refer in a broad sense to sensori-motor Rolandic cortex. The invariable consistency of both motor and sensory sequence, however, indicates that within this general area there are two clearly separable anatomical patterns, one sensory and one motor, and that the sensory and motor elements for each part are closely related to each other.

Stimulation along a zone that crosses the precentral and postcentral convolutions roughly at right angles may activate one of the sensory elements as though circuits in both convolutions were normally involved in the registering of sensation. The same is true of the motor representation although it will be seen in figs. 25A and 29 that motor encroachment upon the postcentral gyrus is infrequent in the inferior half of this gyrus except for a small area adjacent to the fissure of Sylvius. The relative frequency of extension of motor and sensory responses across the central fissure for each region of the body may be seen in figs. 26 and 27. Both motor and sensory points seem to be constant for any one individual, but there is great variation in the topographical position of each point from patient to patient.

Ocular sensation, although rare, does exist. It is usually a sense of movement. This might be expected, a priori, when one considers the fact that there is only sense of pain and sense of position in the eye, and sense of pain has little if any representation in the cortex. These ocular

sensation responses were few in number but were situated anterior to the central fissure as shown by the dotted circles in fig, 30, corresponding with the conjugate eye movements shown in fig. 29.

Ipsilateral response practically does not exist for motor movements. Only in one case out of 126 explorations did an isolated movement occur and that was of the ipsilateral side of the face. But this was produced from outside the Rolandic cortex and was due to the effect of an epileptogenic lesion. Foerster (1936B) also reported that he never obtained ipsilateral response but stated that Penfield had done so. This must have been a misunderstanding.[1] The same is true for sensation, which is always contralateral, not ipsilateral, even in the tongue and face.

Bilateral sensory responses, however, do occur as epigastic aura and head aura. Bilateral sensation occurs also in face, tongue and eyes. Bilateral movement likewise occurs only in eyes, face, tongue and jaw. This bilateral response is in such striking contrast to its complete absence in the extremities that it must indicate a small degree of true representation of bilateral function in each hemisphere.

Displacement of response by secondary facilitation, which has long been known to be possible for motor points in animals, is also possible for sensory points. Occasional great spread of responses over the cortex due to the influence of an epileptic process and the facilitation sometimes produced by that condition is discussed above but will be taken up at greater length in a subsequent publication.

Vocalization (fig. 11) is a phenomenon with well-circumscribed representation in each precentral gyrus. It is made up of a well-formed loud vowel sound which continues until the patient's breath is exhausted, and indeed he may actually begin again after drawing a breath if the stimulation is continued. It is quite distinct from the grunting which has been previously described and which seems to have its representation at a point lower in the Rolandic cortex and nearer the fissure of Sylvius.

Quality of cortical sensation seems to have no particular localization. Numbness and tingling were the descriptive terms most often used. The frequency (forty-nine responses) of sense-of-movement which was predominantly postcentral is of particular interest in view of the desire-to-move which was precentral in distribution (fig. 20). The fact that

[1] This misunderstanding may have resulted from informal conversations with my friend Professor Foerster. At all events I can now corroborate his finding in this regard completely. — W.P.

only eleven times out of well over 800 responses did the patient use the word pain to describe a cortical sensation, probably indicates that pain has little, if any, true cortical representation. The pain was never severe and never caused the patient to object. The diffuse bodily sensations occasionally produced by stimulation of Area 6*a beta* must await further verification from a larger number of cases. The same is true of epigastric aura which seemed to have a localization in the parietal lobe near the mid-line posterior to the postcentral gyrus.

The responses of the cerebral cortex to punctate stimulation are crude. The movements are never dexterous and the sensations are simple, like elements in a Jacksonian march. But however much these responses may caricature true physiological function they nevertheless give insight into the rôle which the sensori-motor cortex must play in the process of integration. And these human records have certain advantages over experimental evidence, for an animal cannot speak and must be anæsthetized, while a patient usually shows a keen, and often impersonal, interest in the activity of his own cerebral cortex.

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COMPRESSION OF THE CHIASMA, OPTIC NERVES, AND OPTIC TRACTS BY INTRACRANIAL ANEURYSMS.

BY GEOFFREY JEFFERSON.

RUPTURE of an intracranial aneurysm has familiarized us with a subject, with a pathology, with a symptom-sign complex which was rapidly fading out of clinical medicine and certainly out of surgery. Time was when aneurysms were a prime differential possibility in any regional surgical diagnosis, and although this is still true, the likelihood of its being the correct interpretation of a clinical problem has become much less during the last fifty years. At the same time our all-round knowledge of aneurysms has considerably advanced and nowhere more than of those within the skull. During the last fifteen years, since indeed the important papers of Beadles, Fearnsides, and notably C. P. Symonds, the neurological world has become so familiarized with the pranks of aneurysmal leakage, and so many important publications have been made upon them, that there might seem to be little reason for traversing so familiar a road. Any such conclusion would be far from the truth, for there are still many blank spaces to be filled. Indeed there is only one outstanding natural experiment of which we can be said to have learned a great deal, and that is the syndrome produced by the sudden effusion of the blood itself into the subarachnoid spaces. But even in this familiar field we still do not know everything. As for the aneurysms themselves, their histological structure, their sites of election and their natural history, we know a good deal and are in process of learning more. It is well established that the pressure exerted by a basal aneurysm may cause paralysis of cranial nerves, amongst others the optic, and the optic pathways. It is with the object of adding something to this side of the picture that the present contribution comes to be made. A search of the literature confirms the fact that amblyopia and field defects are uncommon with aneurysms, for no more than sixty-six cases can be discovered. On the other hand, those here reported for the first time lead to the reflection that the relationship is not quite so uncommon as the figures would indicate. Diagnosis, at one time thought to be beyond human power, has been

made easier by certain important aids, such as angiography, and by the discovery of certain cranial alterations observable on the X-ray film, details of which will transpire as the clinical cases are reviewed.

Accepting the clinical classification of Edwin Bramwell, intracranial aneurysms may present themselves as two types: (*a*) the apoplectic; (*b*) the paralytic. It is with the latter only that I shall deal, and of these this paper will be concerned only with such as have affected the visual apparatus in one way or another, that is by compression of the optic tract, chiasma or optic nerve. Reference will be made in passing to certain other of the ocular signs of aneurysmal hæmorrhage —subhyaloid hæmorrhage and certain subjective visual disturbances occasionally met with in these cases. As for the material, I have records of fifty-three intracranial aneurysms which can be arranged in the following categories: —

1.	Pure subarachnoid hæmorrhage—with nothing to indicate the precise site of the aneurysm	16
2.	Aneurysms with paralysis of cranial nerves, usually the 3rd nerve ..	9
3.	Saccular (non-fistulous) aneurysms of the internal carotid in the cavernous sinus	16
4.	Basal aneurysms with affection of the visual pathways	12

The majority of these aneurysms have been verified in one way or another; in a few the diagnosis is presumptive only, for there was no operative or post-mortem control. (It must be recorded that even with contrast angiography it is not always possible to demonstrate an aneurysm which is certainly present.) The series of cases with an aneurysm in the cavernous sinus will be dealt with elsewhere, for these subclinoid sacculations do not commonly affect the visual pathways unless they erode the optic canal or break into the sella turcica. Such of the subclinoid aneurysms as have affected vision are included here.

Characters of the Aneurysm.

Those cases which fall into the groups (3) and (4) are amongst the most interesting of all, for in these the abnormality of the vessel presents itself clinically as a tumour. In some the suddenness of the onset of symptoms will declare the nature of the lesion, but this is not always the case. In others the growth of an aneurysm has been so slow that it may mimic to a nicety the development of a benign tumour, as indeed it is, save that from the patient's viewpoint a tumour likely to rupture and cause his death in a few seconds can hardly be called entirely "benign." And not only may an aneurysm present a neoplastic syndrome, but it may do worse, and that is, mimic a growth so closely

in gross appearance as to tempt the surgeon to interfere with it too far. Clotting is so common in aneurysms that a structure which should sign its nature by its obvious pulsation is often met with at operation as a solid non-pulsatile mass. There are few hospitals but boast some story of disaster befalling a surgical Mandarin when he made what sounds to be the juvenile mistake of incising an aneurysm. Those more familiar with aneurysms will extend their sympathy, for pulsation may have been imperceptible, the tumour apparently solid. Nevertheless the smoothness of the aneurysmal wall and its freedom from fine capsular vessels is generally sufficient safeguard against mistake. Even if it is incised the dark brown clot contained in it should give an immediate clue to its nature. As will be related below one aneurysm in the present series was tentatively incised and three others were needled with informative results and without mishap.

Compression of the Visual Pathways.

The most important subdivision of carotid trunk aneurysms is that into two classes, supra- and sub-clinoid. The latter are those arising in the cavernous sinus which, as has been said, rarely cause a disturbance of vision. On the whole the clinical picture of these cases is one of ophthalmoplegia with associated disturbance in the trigeminal field. Such visual difficulty as is experienced is due mainly to loss of accommodation by paralysis of the oculomotor nerve or to diplopia. The supra-clinoid aneurysms spring from the carotid at the origin of the ophthalmic or posterior communicating arteries, or at the final bifurcation of the main trunk. With these lesions visual loss is naturally more common.

The relations of the optic nerve, chiasma, and optic tract to the Circle of Willis require brief review in introducing examples of lesions in this situation. The two systems cross one another in such a way that the anterior end of the Circle of Willis lies superior to the chiasma and the optic nerves, whilst its posterior end lies below it and behind it. The grouping of the vessels about the optic nerves and chiasma is so close that an aneurysm arising in almost any vessel can, after primary impingement on the nearest part of the visual pathway, come to compress more distant parts of it and cause progressive changes in the field pattern. Such alteration is an outstanding feature of the aneurysmal syndrome. Thus arises the fact that the linkage between a visual defect and an aneurysm arising from one in particular of the basal arteries is not so succinct, not so uniform in all examples, as might

theoretically have been expected. An aneurysm springing from the carotid soon after it has pierced the dura may compress the optic nerve, or the chiasma, or the optic tract, or combinations of all three. None the less the position of the internal carotid on the outer side of the chiasma is such that monocular blindness or a "junction hemianopia" not only ought to be a common result, but is in fact the most frequent

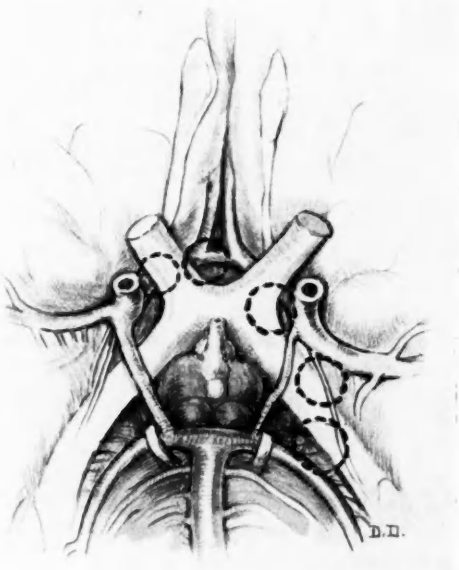

FIG. 1.—Diagram from a normal specimen to illustrate the common sites of aneurysms, and their impingement on the visual apparatus.

single pattern presented. Binasal hemianopia from indentation of both the outer sides of the junction-angle of the chiasma by atherosclerotic arteries has been thought to be a definite entity. It was well figured in a half-forgotten paper by Elliott Smith and from time to time this pathology has been suggested by later writers. There is also the case of Michel figured by Wildbrand and Saenger, and again by Beadles, of cirsoid carotid trunks indenting the chiasmatic junction, but it is a debatable example.

As for the optic tract, examination of the recorded cases proves that a pure tract lesion caused by an aneurysm is a rare occurrence. A glance at figs. 1 and 2 will show that the tract could be compressed by

an aneurysm arising in any branch of the Circle of Willis except, one would say, the anterior cerebral. Yet a case is on record (Harris [42]) in which an aneurysm of this vessel did in fact reach the tract, and it is likely that it suffers more often than has been supposed, but nearly always in combination with a lesion of the chiasma, or of the chiasma and optic nerves as well.

The cases that form the basis of this communication have been grouped under four headings: (1) Those interfering with the optic radiation and striate cortex, 3 cases; (2) those compressing the optic tract, 1 case; (3) those affecting the optic nerves, 2 cases; and (4) those involving the chiasma, 6 cases. It may well be that in some cases an aneurysm compresses more than one part of the visual pathways, but for clarity of analysis and presentation it seems best to make these subdivisions.

The first group call for a word of explanation. Three cases are presented with homonymous hemianopia sparing the macula and greater or less areas of the contralateral field. The sudden onset of the affection and the non-progressive nature of the clinical pictures leaves no doubt that two are examples of thrombosis of the posterior cerebral artery, the third of thrombosis of some part of the middle cerebral. But in all of these cases the immediate clinical picture had been that of subarachnoid hæmorrhage, and it was not until the days of first anxiety on that score were passed that the visual defect was noted. As this picture has not hitherto been described the cases are presented in full.

Group I.—Aneurysms Interfering with the Optic Radiation and Striate Cortex.

Case 1.—Subarachnoid hæmorrhage. Temporary left-sided hemiparesis. Permanent left homonymous hemianopia.

W. B., male, aged 47, was admitted to the Park Hospital, Davyhulme, on July 26, 1935, on reference from Dr. Higson. He had lost the vision in his left eye in a motor accident two years previously. He had attended an annual legal bowling match, and at 4 p.m. he had felt dizzy and had sudden pain in the head and neck attributed to sunstroke. When seen by his own doctor at 8 p.m. he was groaning with pain over the right eye, and vomiting. There was pronounced rigidity of the neck muscles. During the night he became delirious, and next day presented a divergent strabismus. There was great pain on movement of the neck. He was thereupon sent into hospital under Dr. Morrell Roberts, and a lumbar puncture disclosed a heavily blood-stained fluid. I saw him three weeks later. He was remarkably improved but was still drowsy, and at night inconsequent in his conversation. I found a definite

left-sided motor weakness with slight sensory disturbance, and, later, a complete left-sided hemianopia, sparing the macula, in his only seeing eye. The cause of the hemianopia was most probably infarction of the striate area rather than tract compression, for a narrow sector of the superior nasal quadrant was spared, as was an area not more than five degrees in extent around the macula. This is against tract compression, and favours a subsequent thrombosis of the injured vessel. There was no alteration in the optic nerve-head, nor was there ocular palsy. Further lumbar punctures had confirmed the presence of blood diffusely sown in the cerebrospinal fluid. This patient ultimately made a good recovery, the left-sided weakness disappearing though the visual defect remained. In 1936 he had two attacks of minor epilepsy.

The clinical picture was characteristically that of aneurysmal subarachnoid hæmorrhage, but in the absence of anatomical verification the site of the lesion can only be surmised. The oculomotor nerve was not affected in this case. Presumably the aneurysm was small.

Case 2.—Aneurysmal leakage on two occasions. Recovery. Right homonymous hemianopia. Dyslexia. Later, fits.

J. E. A., aged 38, male, in September was talking to some friends whilst sitting at the wheel of his car. He suddenly felt a terrific pain in the left temple as if he had been hit. He was able to drive home and put the car away, but felt extremely ill. He managed to get upstairs and remembered no more except that he was violently sick. The next day he awoke to continued pain and very defective vision, as if he had blinkers on, not being able to see anything unless it was straight ahead of him. Two lumbar punctures were done during the next few days and blood found in the cerebrospinal fluid. He resumed work after a month, but his vision was defective to the right. Three months later he had a second attack, which he recognized as identical with the first, but not quite so severe. Spinal punctures were again performed showing a slight staining with blood. The pain was again in the temple and forehead, an acute pain rather than a headache, lasting two or three days. He vomited on this second occasion even more violently than on the first. After the first attack there was a slight suggestion of difficulty in speech, after the second it was pronounced and was associated with dyslexia. Indeed, it seems likely that a good deal of the difficulty in reading of which he complained was due more to an upset of his appreciation of written language than to his visual defect, which proved to be a fairly congruous right homonymous hemianopia which not only spared the macula but some truncated sectors within 25 degrees in the right homonymous fields. Nine months after his recovery of his second attack he began to have generalized epileptic fits, of which there were five over a period of eighteen months, of decreasing severity, led by an aphasic aura. Apart from the hemianopia and a residual dyslexia, he was an entirely healthy man with no pyramidal or sensory abnormality, and able to carry on his business.

In this case it is not certain whether it was the posterior cerebral or a branch or part of the middle cerebral artery which was at fault.

Case 3.—Mrs. H. C., aged 54, referred by Mr. Sumner, of Preston, with a right-sided homonymous congruous hemianopia, dated her symptoms from an attack of "sunstroke" eleven years ago. She had been taking up bulbs in her garden and was suddenly struck by a violent pain in her neck. She was found lying on the path unconscious. She recovered in a few minutes and vomited. She was confined to bed in a darkened room for two weeks, vomiting occasionally, with excruciating pain in the head and back of the neck. She made a very slow recovery and discovered eventually the loss of vision to the right side. An interesting more recent feature has been the development of special-sense epilepsy, attacks with a visual aura. She sees extremely bright stars moving in the right field, definitely formed, some two inches in size with points like a formal star figure. They are so bright and dazzling that she can see little whilst they are present, which may be for several minutes. She feels very upset for two or three hours afterwards. In this case the sudden onset of violent occipital and nuchal pain with vomiting leave one with little doubt that the original "stroke" was an aneurysmal leakage from the left posterior cerebral artery followed by thrombosis of the vessel. From my own experience of these cases, it seems that epilepsy is a curiously common sequel of thrombosis of the posterior cerebral artery ("scar epilepsy"). She has a right-sided homonymous hemianopia sparing the macula.

These three cases raise the very interesting point already alluded to —relationship of posterior cerebral arterial thrombosis to aneurysm. It is true that thrombosis sometimes occurs for no discernible reason (e.g. phlebitis migrans), but thrombosis in normal arteries is so rare a happening that it is proper to search for a cause. May it not be that it is sometimes the presence of a congenital defect in the vessel wall, an aneurysm? It is quite certain that aneurysms thrombose and that the territory of their supply becomes endangered by ischæmia. This is a commonplace with aneurysms of the limbs, and no doubt is equally true of the intracranial vessels. In the cases recorded above the visual field pictures suggest infarction of area striata rather than tract compression. Symonds [80] has twice observed compression of the optic radiation by false sacs originating in posterior cerebral aneurysms, and this mechanism is a definite alternative to pure ischæmia. However this may be, the fact of the happening is important and more cases of posterior cerebral thrombosis may in the future be found to be due to this cause.

In the literature homonymous hemianopia of aneurysmal origin has been described seven times (*see* Table of collected cases). In most of

these cases there was tract compression, as in my own Case 4, or so one presumes. When a hemianopia results from an aneurysm of the carotid trunk rather than the posterior cerebral the field defect must be due to pressure on the tract and not to infarction of the occipital lobe. Only one aneurysm of the posterior cerebral artery of real importance is described in the literature, Byrom Bramwell's Case 3, but it is not included in this paper because no studies of the visual fields had been made, or perhaps, had been possible, for the patient was severely damaged mentally. The visual defect is not mentioned in Squire's case [77].

Group 2.—Compression of the Optic Tract.

Case 4.—Aneurysm of right posterior cerebral artery, third nerve palsy, left homonymous hemianopia, left-sided hemiparesis, anæsthesia of right trigeminus.

A. L., aged 29, female, was admitted to Salford Royal Hospital, November 18, 1927. For six months past the patient had felt depressed, headachy and unusually sleepy. Menstruation was not affected. She slept at any time during the day when opportunity presented. During this time she had had frequent visual hallucinations in her left field as of glittering golden buttons which she would try to touch with her hand. Three weeks before admission very severe bitemporal headache suddenly developed, and severe occipital pain. So bad did this become that she was unable to sleep, and she became blind in both eyes for twenty-four hours (probably from hæmorrhage into the sheaths of the optic nerves and subhyaloid exudate). There followed a slow improvement in vision, but she had not been able to see to the left since. Three days after the sudden access of pain the left side of her body became weak, but not paralysed. For the past seven days she had had ptosis of the right upper lid. On admission she was in great pain all over the head, with slight rigidity of the neck. The discs were normal. She presented an incomplete third nerve palsy on the right side with hypæsthesia over the right trigeminal field. There was a complete left homonymous hemianopia with split macula to confrontation, so far as could be accurately judged. She had a left-sided hemiparesis of mild grade with the usual evidences of an organic pyramidal lesion. Lumbar puncture gave a faintly blood-stained fluid with a slightly yellowish background. The diagnosis arrived at was an intracranial aneurysm of the posterior portion of the circle of Willis. It seemed unlikely that anything really useful could be done for her, for it could be by no means certain that the aneurysm sprang from the carotid, hence its ligature would be of very uncertain issue.

An intracranial exploration was done three days after admission because, chiefly, of the intense pain of which she complained. This showed no evidence of bleeding and a decompression was made. Events were to prove than an aneurysm was there, but in a most inaccessible position. Her headache after

this was rather less, but as time passed her oculo motor palsies became more profound on the right side, her face more deeply anæsthetic, whilst a discriminatory sensory loss made its appearance on the left side of the body. The hemiparesis did not materially deepen, and she improved sufficiently to sit out of bed until, on Christmas Eve, she was suddenly seized with violent pain in the head, became unconscious, and died in five hours. At necropsy an

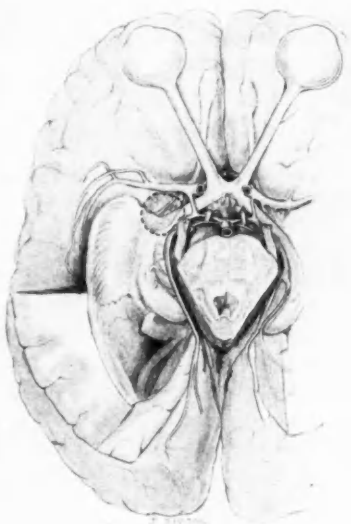

FIG. 2.—Schematic drawing from specimen (Case 4).

aneurysm the size of a pigeon's egg was found arising from the posterior cerebral artery immediately outside the third nerve (*see* fig. 2). It indented the crus cerebri and optic tract and was perfectly placed to produce a full-fledged Weber's syndrome. The mechanism of production of the trigeminal anæsthesia was by compression of the edge of the tentorium overlying the forward passage of the sensory root. The aneurysm had ruptured into the right lateral ventricle through the chorioidal fissure.

Comment.—The vessel most favourably situated to cause a lesion of the optic tract is the posterior communicating, but aneurysms of this artery are generally small and probably they rupture before they have indented it enough to give rise to recognizable visual disturbance. The tract is most often damaged by a blow-out on the internal carotid trunk

or the middle cerebral near its origin (*see* figs. 1 and 2). In Gordon Holmes' case, recorded by S. T. Harris, an aneurysm of the anterior cerebral had not only compressed the chiasma but passed back to stretch the right optic tract over it.

Compression of the Optic Nerves.

The close relationship between the optic nerve and the internal carotid artery at the anterior clinoid process should be a very cogent reason for unilateral visual loss in carotid aneurysm, and this proves to be the commonest result, judged by the reported cases.

Case 5.—Aneurysm of the internal carotid artery in the anterior end of the left cavernous sinus. Defective vision in the left eye.

M. A., aged 50, female, was admitted to the Salford Royal Hospital, November 14, 1932. She was an emaciated woman who had to give up work twelve months previously because of fatigue and mental instability. However, there were obvious clinical signs suggesting a space-occupying lesion. She

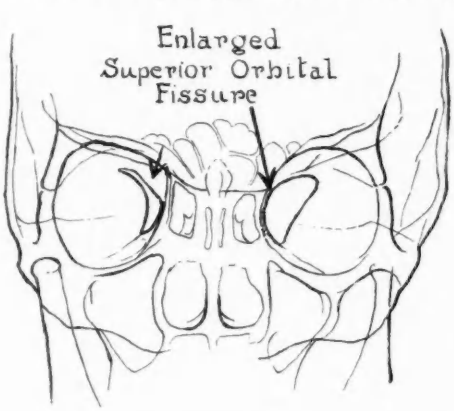

Fig. 3.—Drawing from radiograph (Case 5), showing enlarged superior orbital fissure on side of aneurysm.

feared "an evil spirit moving in her inside" and this she feared would "go to her head." She had been quarrelsome with, and suspicious of, her fellow workers in a large store in which she held a position of trust. It proved impossible to get a connected history from her, but the following facts were established. Five years ago she had experienced paræsthesia of the left side of her face, one year ago it became numb. During the last few months the left eye had slowly closed. She complained of dull left-sided headache. Examination showed a complete left third palsy, pupil mid-dilated, immobile, and the left abducens acting, but not fully. The left disc was paler than the normal

right, but was not atrophic. V.A.R. $\frac{6}{9}$, V.A.L. $\frac{6}{6}$. Fields could not be taken owing to poor co-operation, but there seemed to be no significant defect. Anæsthesia was present over the whole left trigeminal field with areflexia cornealis: paralysis of motor branch of left trigeminus. Slight pyramidal signs were present on the right side of the body: abdominal reflexes present but exhaustible on the right, increased tendon reflectivity on the right side, plantars flexor. No impairment of sensation could be established over the body and limbs. There was no bruit on auscultation of the head. X-ray showed enlargement of the sphenoidal fissure on the left side with evident erosion of the greater wing of the sphenoid (*see* fig. 3). In the lateral view Dr. Morris reported a faint large shadow, with definite edges, occupying the floor of the middle fossa on the right side behind the sphenoidal wing. The pituitary fossa was not eroded.

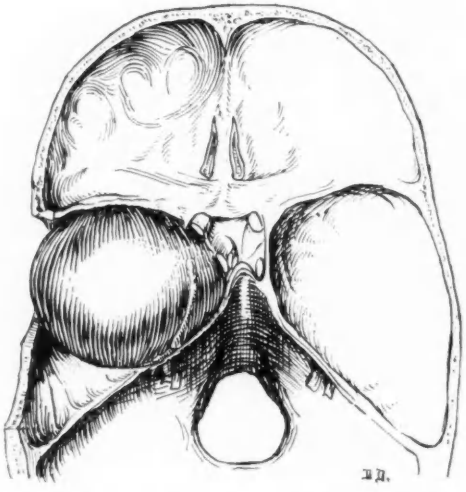

FIG. 4.—Saccular aneurysm of internal carotid filling middle fossa (Case 5).

Comment.—There could be little doubt as to the anatomical situation of the lesion present in this case. The diagnosis was not so certain. Several cases of massive carotid aneurysm had already been studied; in all of them the onset of symptoms had been abrupt. In this case there was a five-year history of an affection of the whole trigeminal field, followed later by unilateral oculomotor palsies, a group of signs so characteristic of aneurysm that this diagnosis was reached. The shadow seen in the X-ray was also in favour of this entity, though it was unlike the common shell-like aneurysmal picture. It was evidently a variant

of the more ordinary capsular type of calcification that gives the ring shadow recorded by many people, amongst others Albl.

Operation was undertaken to verify the lesion. On December 28, 1932, a small osteoplastic flap was cut under local anæsthesia in the left temporal region, cutting the edges straight so as to get it to break low down (Lambert Rogers). Dura very tense. Intravenous hypertonic saline was injected at the ankle. The dura was opened and found adherent to underlying cortex. The Sylvian fissure was considerably elevated. Beneath a thin shell of temporal cortex a resistant mass could be detected, at first suggesting a meningioma. It was exposed by excising a small portion of the second and third temporal gyri. The wall was smooth and greyish, entirely devoid of vessels. Palpation revealed it to be pulpy and of very considerable dimensions though its full extent could not be determined without damaging the brain. A sharp needle was inserted into the tumour; dirty brown fluid was at first

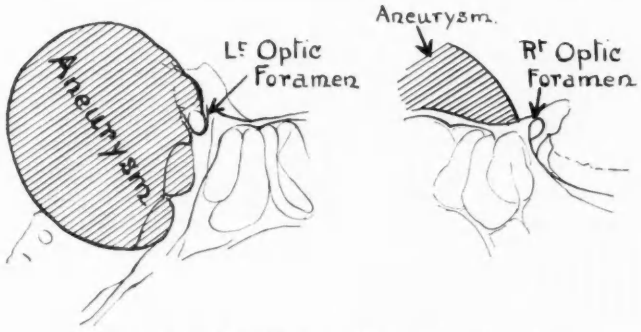

FIG. 5.—Elevation of optic canal by aneurysm (Case 5).

obtained, but at a depth of 4 cm. bright arterial blood filled the syringe. On withdrawing the needle a high but very narrow stream of bright arterial blood issued from the puncture hole. This was at once controlled by placement of a hot moist pledget of cotton on to the puncture and leaving it undisturbed for ten minutes. Bleeding was then found to be completely arrested and the flap was replaced.

The operation was well borne but the right-sided weakness became progressively more marked and she died thirty-five days after exploration. A huge aneurysm, almost completely thrombosed, was found lying in the whole of the left middle fossa from the wing of the sphenoid anteriorly to the petrous bone behind (fig. 4). It had destroyed the left temporal lobe, only a shell remaining. The aneurysm arose from the intra-cavernous portion of the left internal carotid artery and had compressed the ipsilateral Gasserian ganglion and all the left oculo motor nerves. It eroded into the air sinuses anteriorly. Studies of the optic foramina in this case were made for me at a later date by

Dr. Twining. They show an alteration which we have found to be clinically important (fig. 5) and which calls for immediate comment.

The radiographic alterations.—The striking things were the enlargement of the spenoidal (superior orbital) fissure as seen in the antero-posterior view. In addition to this the bridge of bone which passes from the body of the sphenoid to the lesser wing and forms the lower and outer boundary of the optic canal is seen to be thinned. This also is a characteristic aneurysmal sign, and further examples will be shown. The optic canal has in this case been elevated, and it is surprising that with so much change nearby the visual disturbance was not more pronounced. Many observers have been impressed by the preservation of vision in cases where the nerve had looked to be considerably embarrassed by contact with an aneurysm. It was unfortunate that her mental condition precluded more detailed visual studies.

I have one other case with monocular amaurosis, this time of sudden onset.

Case 6.—Vomiting followed by severe pains in the face and trigeminal anæsthesia. Development of ptosis. Coarse visual hallucinations of light and then blindness.

M. F., aged 60, female. On October 1, 1930, she was suddenly seized with vomiting, which continued unabated for three days. On October 5 she experienced severe neuralgic pains in the left side of the face in all three divisions: the pain, to use her own expression, swept over her face like waves of liquid fire, and was intense in the eyeball proper. This ceased after forty-eight hours, but left some tingling in the face. During the night a ball of yellow light appeared before the left eye, burning with great intensity, and in the morning the sight was almost gone. Three days later she was found to be completely blind. She had an immature cataract in this eye and a corneal opacity in the other. On October 7 the left eyelid began to droop and in a few hours the eye closed completely. When seen with her family doctor she was found to have a complete left-sided ptosis and opthalmoplegia, no movements of the eyeball were possible. There was fairly dense anæsthesia of the whole left trigeminal area. She was again experiencing shoots of pain, chiefly in the ophthalmic division, sometimes into the mandibular, and into the ear. There was no weakness on the limbs, and mentally she was clear. Glimpses of the retina were obtained and what could be seen was normal. The patient absolutely refused to enter hospital or to have any further investigations carried out. She was lost sight of except that it was learned that she had survived for some weeks at least, and moved to another part of the country.

Comment.—This is an imperfect case in that there is no verification of the lesion. But the history is so strongly suggestive of aneurysm that this diagnosis will be hard to refute. The sudden development of her catastrophies is strongly in favour of a vascular origin. There were no

signs indicative of a subarachnoid or intracerebral hæmorrhage, whilst everything can be perfectly well explained by the sudden blowing out of an aneurysm of the internal carotid artery in the cavernous sinus. It must have been large for it damaged the whole of the trigeminus, indicating that it extended well back in the sinus; on the other hand it extended far enough forwards to damage vision. By exactly what mechanism this last effect was produced must remain conjectural, whether by direct compression or by embolism. The former is more likely as blindness occurred before detachable clot formation was probable. The visual hallucination was an interesting point in this case. It had already been noted in two of the present series (Cases 4 and 5) and will be observable again in a later one, where the compression of the optic nerve was confirmed at operation. There are six other cases of blindness amongst the collected cases, one of the most authentic being that of Wildbrand and Saenger. In Jonathan Hutchinson, junr.'s case there was hæmorrhage into the retina (and subhyaloid hæmorrhage can, of course, cause temporary blindness) but at post-mortem a large basilar aneurysm was found extending forwards to compress the chiasma. As a rule the aneurysms have arisen from the internal carotid and have injured the chiasma severely.

Chiasmal Compression.

Anterior Cerebral Artery Group.

It has already been said that chiasmal compression is produced by abnormality of the anterior rather than the posterior end of the circle of Willis. The vessels best placed to cause a chiasmatic field defect are the anterior cerebrals and their communicating artery. These trunks lie above the chiasma and so close is their relationship that elevation of the chiasma from below by a pituitary adenoma may cause the vessels to cut into the dorsal chiasmal surface and produce a variant of the typical pituitary field defect. It is probable that the loss of the lower nasal quadrant, seen in advanced cases of pituitary enlargement, is generally caused by this vascular addition to the neural embarrassment, and not by pressure from the upper edges of the optic canals. Conversely, an aneurysm arising from the anterior cerebral vessels indents the chiasma from above and nestles into its now concave upper surface. It will lead to a variable picture according to its placement either exactly in the mid-line or eccentrically slightly to one or the other side, when one nerve will suffer more than the other. It is

important to recognize that the situation of these particular aneurysms renders them incapable of producing cranial nerve palsies, other than optic or olfactory. This was not true of aneurysms in the posterior portion of the basal circle of arteries. The suprachiasmatic aneurysm is entirely intradural and buries itself in the under surface of the frontal lobes. The only other nerve that it has an opportunity of affecting is the olfactory pair, but they are sufficiently lateral to escape in most cases, so that anosmia is rare. These aneurysms give a difficult clinical picture. They often evolve slowly, and behave like the tumours that they indeed are. It must be added that a very sudden appearance or worsening of symptoms is more common in aneurysmal enlargements than in any other tumour. More characteristic still is the rapid improvement in vision after a sudden, often monocular, depression of acuity, a point well illustrated by the case which follows and even better by Conway's [16].

Case 7.—*Aneurysm of the anterior cerebral artery. Supra-chiasmal compression. Operative verification.*

E. K., aged 36, female, was admitted to the Neuro-Surgical Service of the Manchester Royal Infirmary from Dr. Fergus Ferguson, August 22, 1933, with the diagnosis of chiasmal lesion, probably aneurysmal. For seven months past she had suffered from headaches, to which she had been unaccustomed. At first left-sided they had spread all over her head. She characterized the headache as terrific, constantly there in some form, but blazing up with very violent pain for half an hour or more. Three months ago when the pain was unusually severe, she vomited continuously for five days. For four months past her vision had been failing in the left eye. There were no other complaints except for uncinate attacks, four months ago during one week, when she had intermittent subjective smells of decaying cabbage. There had been no return of it. On examination she was an apparently healthy woman of average build. V.A.R. $\frac{6}{5}$, V.A.L. $\frac{6}{18}$. Pallor of left disc, right normal. No anosmia. Visual fields showed a normal right field, in the left there was a paracæcal scotoma drifting towards the macula. Macular vision was somewhat affected, the fixation point fading and coming back during testing, but the peripheral field was normal. The X-ray of the sella showed no change. There were no other signs, no pyramidal or character changes.

Clearly this was not a pituitary tumour; she had too much pain for a chromophobe adenoma. Even with a normal sella she might have had a supra-sellar adenoma, but the patient seemed to be too ill for this. A meningioma of tuberculum sellæ was less likely even than an adenoma, for severe headache is rare with them and the history was too short. After having worried over this case for some time, nothing was done, and she was allowed to go home.

Seen in the out-patients two months later, she declared that her pain was

even worse than before and that her vision was failing more definitely. The acuity in both eyes had gone down severely, V.A.R. $\frac{6}{24}$, V.A.L. $\frac{6}{18}$. Her fields now showed a suggestive hemianopia in the smaller isopters and to colour (fig. 6). Menstruation continued regular. Diagnosis was coming nearer. She was readmitted to hospital after some delay, in January, and was found to be visually much worse, V.A.R. 0, V.A.L. $\frac{6}{18}$. This was a remarkable change,

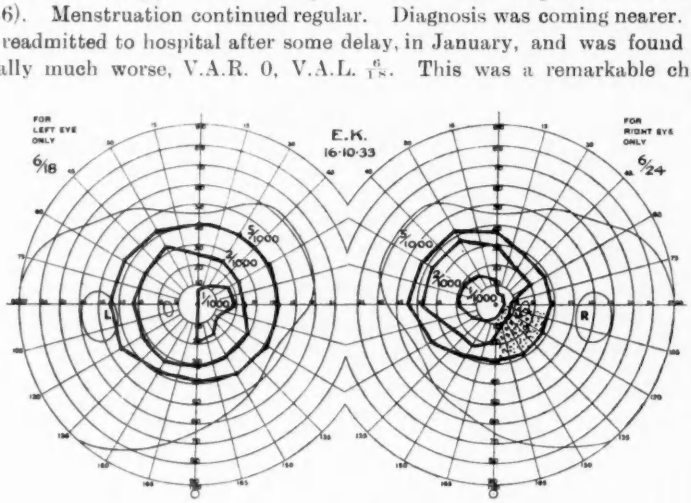

FIG. 6.—Visual fields (Case 6).

for her left eye had been her worse, and now vision had gone on the right. The left field was interesting for it presented a lower temporal defect, changing to a hemianopia with a 1 mm. white disc (fig. 7). This strongly suggested a supra-chiasmal lesion. There was no anosmia, no ocular palsies, trigeminal fields normal, corneal sensation perfect. Bilateral optic pallor was now present with normal vessels. No pyramidal signs. X-ray of sella again showed no alteration. Optic canals normal. Cerebrospinal fluid protein, 40 mgm. B.M.R. normal (—6). Blood-urea and blood-sugar, normal. Wassermann reaction negative.

Operation.—January 16, 1934, under local anæsthesia, later helped out by ether.

Trotter flap. Uneventful exposure. The dura was elevated without incident and incised along the lesser wing of sphenoid; the pressure was low, moderate amount of fluid. Dissection around the right optic nerves was painful, first referred to the eye and later to the top of the head. The nerve was difficult to bring into view due to a thickened arachnoid. The adhesions were separated and finally a tumour was glimpsed above and to the inner side of the right optic nerve. Gradually, as arachnoid adhesions were divided, a rounded smooth-walled cystic tumour became visible, dark in colour (fig. 8). A little dissection freed it below and the inner side of the left optic nerve was seen and partly cleared. No pulsation was felt. At this point a fine hollow

needle was inserted but nothing could be withdrawn, which was surprising as the "tumour" was clearly very soft. An incision 1·25 cm. long was made in the wall of the swelling. There was no escape of contents. A small curette inserted brought out a small quantity of brown material that looked like clot,

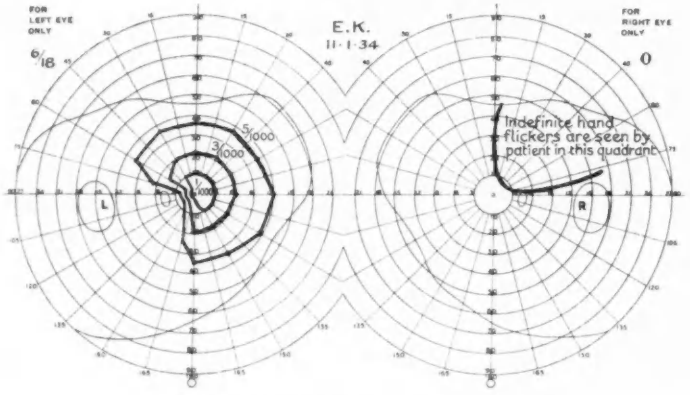

FIG. 7.—Visual fields (Case 6), three months later.

and in a few moments there was a rush of bright blood that was instantly stopped by wet lintine packing, on the front of what was now clearly a large aneurysmal sac. The material removed was sent to the laboratory and an immediate report returned that microscopically it consisted of old clot. The

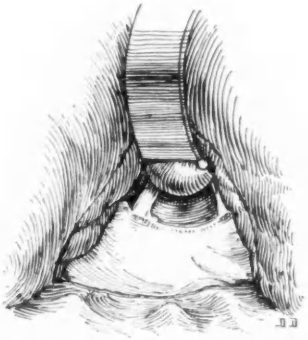

FIG. 8.—Case 6, operation sketch of supra-chiasmal aneurysm.

cotton was left in situ for fifteen minutes undisturbed, and on removing it the field was dry. Muscle grafts were packed on to the front wall of the aneurysm. The wound was closed as usual. Intervention well borne, pulse and pressure

unaltered. Two weeks after the discovery of the aneurysm bilateral thorotrast injections were made in order to visualize the vessel causing the lesion. Although good pictures were obtained no sign of an aneurysm could be seen. On injection of the left internal carotid she had a temporary attack of aphasia and right-sided paresis which fortunately passed off in ten minutes. The vessel had contracted down on puncture to a narrow cord, and the signs were attributed to severe carotid vasospasm.

Following on this the patient was improved, her headache diminished and there was general physical improvement, possibly because of the mobilization of the aneurysm. She was seen from time to time during the next year. Vision remained unchanged. Eighteen months later she returned home one day from shopping, felt very ill and went upstairs to lie down. Here her husband found her dead when he came home from work. Post-mortem examination discovered an aneurysm of the right anterior cerebral artery at its junction with its communicating branch. It had ruptured into the anterior horn of the ventricle. The aneurysm measured 4 cm. in diameter and was completely thrombosed, except above, where a very thin-walled sac contained fluid blood, and was the site of rupture.

Comment.—This case was a particularly valuable one, as we were able to follow the evolution of her chiasmal compression over most of its active course. Beginning with a paracæcal scotoma and depressed acuity in the left eye, the picture changed first to a suggestive bitemporal hemianopia, with a sudden reduction of acuity in the previously better eye, and then to blindness in that eye, with an inferior temporal defect, but improved acuity, on the originally worse side. The relatively rapid evolution of the changes, the extremely severe pain, the normal sella, the circumscription of the lesion, all fitted perfectly with the lesion that was finally discovered embedded on the dorsal surface of the chiasma and optic nerves.

The removal of the aneurysm was a tempting idea but it was decided, and I think correctly, that carotid ligature would be no use, and that control of hæmorrhage during removal would be so uncertain as to make it too hazardous.

Case 8.—Supra-sellar aneurysm. Blind right eye, temporal hemianopia in the left. Calcified shell visible in radiograms. Thorotrast verification. No operation.

E. S., female, aged 49, was admitted to the National Hospital under Dr. Denis Brinton, November, 1935, blind in the right eye and with failing vision in the left. Eight years ago she began to suffer from persistent frontal headache, chiefly right-sided and never very severe. Her vision began to fail in the right eye, first in the temporal field, which went, she felt certain, from

below upwards. She consulted specialists but no diagnosis was arrived at, and in the space of two years the eye became blind. Two years later, in July, 1931, vision began to be affected in the left eye, again in the lower temporal quadrant. During the ensuing four years there was a slow advancement to

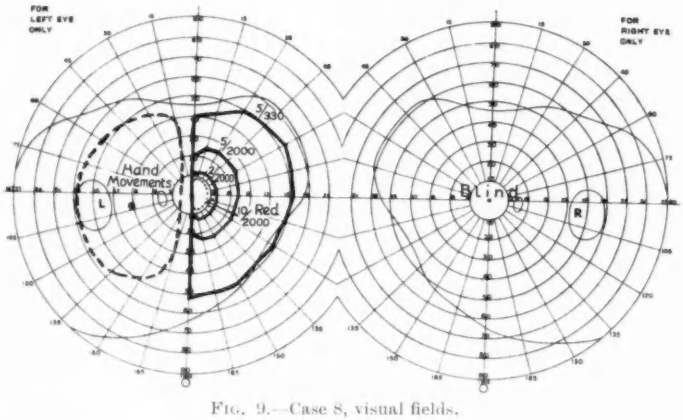

FIG. 9.—Case 8, visual fields.

her present condition. She had had no headache during the last three years. Menstruation, irregular after 45, had ceased after 48. There was no evidence of pituitary dysfunction and no tuberal signs. She was a spare woman, intelligent, interested, concerned lest her left eye should follow the same course

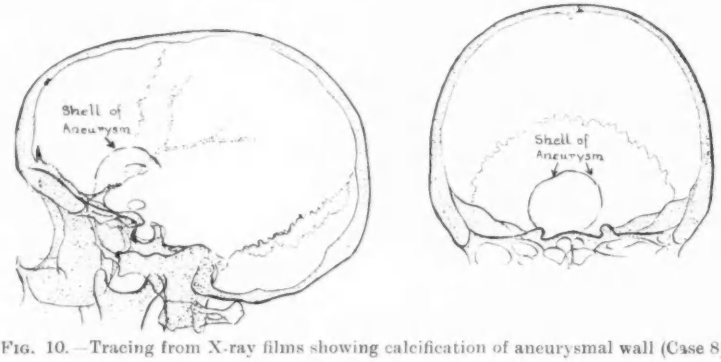

FIG. 10.—Tracing from X-ray films showing calcification of aneurysmal wall (Case 8).

as had the right. No anosmia. There was high grade primary atrophy in the right eye, which was blind. No light reflex. V.A.L. $\frac{6}{18}$, with definite pallor of periphery of disc. There was no external ocular palsies. Corneal sensation normal. Trigeminal fields normal. The left visual field showed a complete

temporal hemianopia sparing the macula: hand movements were vaguely perceived in the temporal field (fig. 9).

X-ray.—Sella normal. Above and rather in front of the sella was a fine shell of calcification visible in all views (fig. 10). The upper edge was 5 cm. above the sellar floor; in the antero-posterior view it was 4 cm. wide. It was high above the sella and incomplete. The appearance was highly suggestive of calcification in the wall of the aneurysm. There were no other signs. Serological tests negative.

Comment.—Judged from the patient's own description of the early field losses, it seemed certain that the lesion was suprachiasmatic. At the time of observation the one thing that was sure was that she had a clean-cut temporal defect in her only seeing eye. The shadow above

FIG. 11.—Case 8, Angiogram of left carotid aneurysm.

the sella was too high for a calcified Rathke pouch tumour and the sella had not been disturbed by pressure. The likelihood was that this tumour was aneurysmal, and had arisen from the anterial cerebral artery just above its origin from the internal carotid. It had then passed inwards above the chiasma, slowly developing into the large tumour now visible.

In order, if possible, to make sure of this, angiograms were made.

Operation: November 7, 1935. Bilateral thorotrast injections were made by the writer with Mr. Harvey Jackson. A small tuft of thorotrast could be seen entering the aneurysm from the left side at the origin of the anterior cerebral artery (*see* fig. 11). So small a filling was disappointing considering the size of the aneurysm, but it must be remembered that we are only now beginning to be familiar with the appearance of angiograms of aneurysms in the living. Post-mortem specimens have accustomed us to the fact that aneurysmal sacs are generally more or less filled with laminated clot, and that the amount of blood which they can contain is considerably less than their external size would indicate. There is no doubt whatever that the lesion in this case was aneurysmal. No further operation was performed. Her vision was so precarious that it seemed possible that anything that might be done might make her blind. Even carotid ligature was not quite immune from this risk.

It was curious that although her vision went first in the right eye, that the aneurysm was proved to spring from the left side.

In the next case, though the degree of filling obtained with thorotrast was small, there is little doubt that the lesion is also aneurysmal, for the fields proclaim it in conjunction with the calcification visible in the radiograms, and the notable change in the sphenoidal fissure and optic foramen.

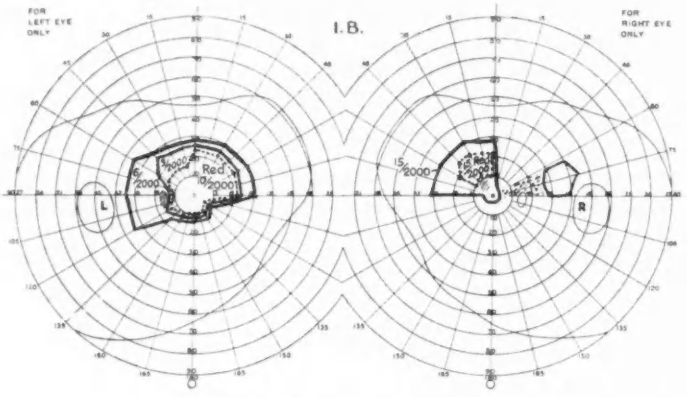

FIG. 12.—Visual fields of Case 9.

Case 9.—I. B., aged 59, male, was referred to the Neuro-Surgical Service, Manchester Royal Infirmary, by Dr. Hamer, of Ashton-under-Lyne.

A previously healthy cotton-spinner (but for hypochromic anæmia two years ago). Six months previously vision in both eyes had decreased suddenly at about 11 a.m. one morning. The interior of the mill looked misty, and objects

were not clear. There was no pain, though the eyeballs felt a little sore. The dimness had not increased since he first noticed it, but he had not been able to see clearly enough to allow him to work. He had not been conscious of any pattern in his visual loss, the right eye was much worse than the left. On examination there was nothing remarkable except his general rather yellowish pallor. Blood-count: 3,560,000 erythrocytes, colour-index 0·99, slight aniso- and poikilocytosis, no nucleated red cells. Sugar curve, normal. Metabolic rate, normal (+7). Cerebrospinal fluid, nothing significant, albumin 35 mgm. Bilateral optic atrophy, disc edges well defined, vessels normal. V.A.R. $\frac{1}{60}$, V.A.L. $\frac{6}{24}$. Fields showed an incomplete altitudinal hemianopia in the left, and on the right vision was preserved only in the nasal quadrant and macula, save for a few flickers visible in the upper temporal field (*see* fig. 12).

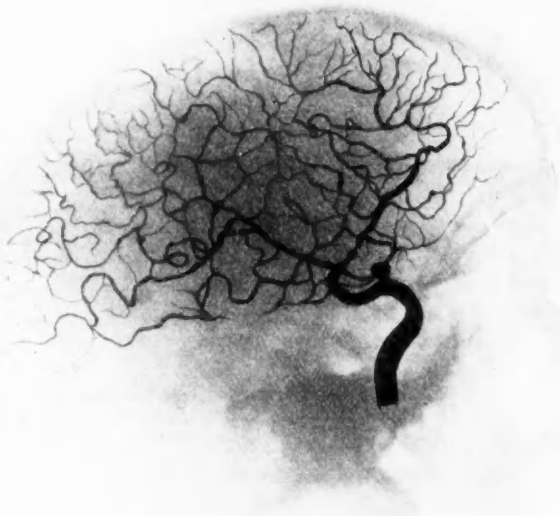

Fig. 13.—Angiogram of Case 9.

X-*ray*.—A fine line of calcification arose from the sella and curved down again to the tuberculum. The sella itself was completely destroyed posteriorly. Oblique views through the orbits showed an unusual change in the right optic foramen, the lower and outer wall being absent. In addition, the inner end of the sphenoidal fissure was seen to be enlarged, a point in favour of aneurysm, as already well seen in Case 3. These points are, however, subsidiary to other important features in this case. The first is the abruptness of the amblyopia (*cf.* the case of Wildbrand and Saenger), the second is the clearly altitudinal

nature of the hemianopia with an inferior defect. Even in the almost blind eye the upper temporal field is clearly scotomatous, flickers being still discerned and a patch of vision is almost chartable. This was not true of the inferior fields of either eye. The lesion is evidently suprachiasmal and nests in the dorsal surface of the chiasma. The aneurysm has probably arisen from one anterior cerebral artery, the right if the more injured nerve is a guide (but see the preceding case). If the aneurysm arises from an anterior cerebral, it is possible that it will not fill with thorotrast (*see* Case 8 above, in which an operatively verified aneurysm failed to do so). Angiograms were made, and show an abnormal tuft of thorotrast approximately at the region of the anterior cerebral artery (fig. 13).

Internal Carotid Group.

In the remaining three cases of this series the chiasmal syndrome was produced by an aneurysm of the internal carotid insinuating itself into the sella in a medial direction.

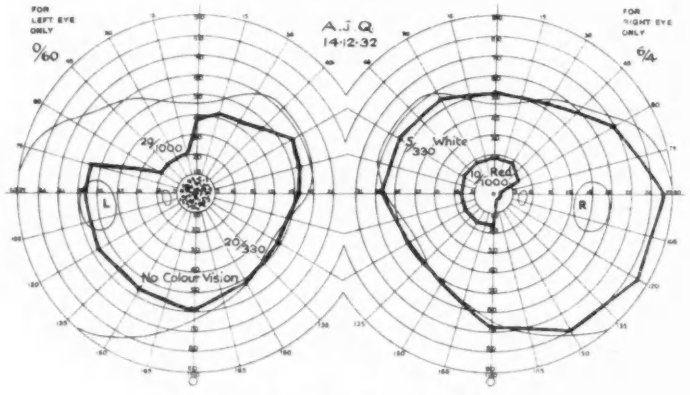

FIG. 14.—Visual fields of Case 10.

Case 10.—*Sudden onset of amblyopia in left eye. Severe headache, partial destruction of sella turcica. Pallor of optic discs.*

A. J. Q., aged 56, female, school mistress, was referred by Dr. Fleming of Liverpool with failing vision in the left eye. For twenty years she had suffered from left-sided periodic headache. Between the ages of 30 and 39 she had nervous breakdowns, in the worst of which her memory forsook her. This was attributed to the strain of teaching. For several years her health had improved. Five months ago, when in bed one night, a bright light glittered suddenly in the left eye and continued for some minutes so that she could not see. Next morning there was internal strabismus in this eye, and it has persisted since; though vision returned, from that day onwards it had slowly deteriorated.

White images floated before this eye, always of the same size and shape. Anything bright on her left side seemed to glitter and sparkle. She has had considerable pain in the left globus oculi and also in the forehead on that side, and again in the cheek below the eye, occasionally in the maxillary teeth, more rarely in the temple. Menstruation ceased six years previously.

On examination.—A very nervous woman of good average physique. She had a radiographically proved gastric ulcer on the lesser curve. There was a left-sided abducens palsy. The left optic nerve head was pale but not atrophic, yet vision was down to finger-counting; V.A.R. $\frac{6}{4}$. Her visual fields showed an upper temporal quadrantic defect in the left eye, where a 20 mm. test object was seen as a small, dull misty dazzle. The right field was full to 5 mm. white,

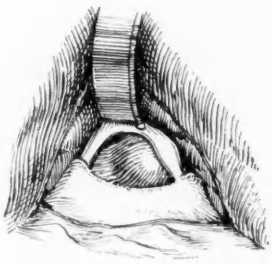

FIG. 15.—Operation sketch of carotid aneurysm, compressing left optic nerve (Case 10).

but there was a suggestion of temporal hemianopia to colour (fig. 14). X-ray showed considerable enlargement of the sella, but the type was not very suggestive of pituitary adenoma, there was too much destruction of the dorsum sellæ. All serological tests were negative. Metabolic rate normal (+ 2). No anæsthesia anywhere in the trigeminal field. Diagnosis was by no means easy. The fields were unusual for a pituitary adenoma. Even allowing for compression of the left optic nerve by a nubbin of tumour burst through the capsule, the right field was unusually free from defect, though there was just a suggestion of colour hemianopia. The lesion clearly falls most heavily on the one optic nerve. The dorsum sellæ was broken off and damaged to a degree in excess of expectation, having regard to the short history. Aneurysm seemed to be a possibility, especially in view of the sudden worsening of vision on a night six months ago. That again could have been due to a hæmorrhage into a pituitary tumour, but scarcely with so little change in the field of the right eye. On the whole the eccentricity of the clinical picture favoured aneurysm.

Operation.—On December 17, 1932, a left-sided frontal flap was turned down (i.e. on the side of the worse vision), and an extradural approach made to the optic nerve. When the nerve was brought into view it was seen to be stretched over a small rounded tumour that projected to its inner side (fig. 15). This swelling did not reach the right optic nerve, nor did it extend far back.

It was dural-clad and clearly was not a pituitary adenoma. There was no sign of pulsation in it; it was dark, and there were no vessels in its capsule. It was decided to aspirate its contents, to discern its nature. A fine long Labat needle was introduced into the tumour. Bright arterial blood was obtained on aspiration. On withdrawing the needle a narrow stream of bright arterial blood spurted from the puncture hole beyond the operation field. Clearly, the tumour was an aneurysm. A pledget of wet cotton placed upon the puncture at once controlled the bleeding, whilst a small muscle graft was cut from the temporalis. This was exchanged for the pledget and held in position for several minutes. The wound was washed out with Ringer's solution and the graft seen to adhere perfectly. The wound was closed. The aneurysm had sprung, in all likelihood, from the last portion of the internal carotid, at the point where it gives off the ophthalmic artery. The problem now arose as to whether to tie the carotid or not. As the aneurysm was well covered with dura it was thought that rupture was not an immediate danger. The problem was left for discussion with the patient, who decided against ligature. Five years later she is still alive and fairly well but for her gastric ulcer. There is no interference with the sight in her right eye. This patient was heard from in October, 1937; she says that there has been no alteration in the vision in her right eye, and that she is fairly well and has no pain.

Comment.—This was a perfect case of unilateral optic nerve compression by an aneurysm. It is possible, but not probable, that her migrainous headaches of many years standing had this lesion as their basis. Severe monocular defect is not uncommon in irregular contoured pituitary adenomas, but I have not yet met with an adenoma in which a more definite field defect has not been present in the other eye at the same time.

Case 11.—*Chiasmal syndrome. Enlarged sella turcica. Alteration in lower and outer rim of optic foramen. Operation. Ligature of internal carotid. Great improvement in vision.*

T. T., aged 23, male, was referred to the Neuro-Surgical Service of the Manchester Royal Infirmary on August 31, 1935, by Mr. Bamford, of Derby, with the diagnosis of chiasmal lesion. Eight months ago he was reading, and by chance discovered that he could not see with his left eye. He consulted Mr. Bamford, who found suggestive defects in the visual fields. Vision in the right eye had failed rapidly and he could only read for two or three minutes at a time owing to blurring of sight. He had had no pain to speak of. There was no other complaint. He was an obese man with a very smooth skin and fine hair, and a physique very suggestive of a chromophobe adenoma. B.M.R. −11. Neurological examination was negative apart from vision. No disturbance of the autonomic centres. Not impotent.

The visual fields showed a clean-cut bitemporal hemianopia, with the macula just spared (fig. 16). Visual acuity, right $\frac{6}{18}$, left $\frac{1}{60}$.

X-rays of the sella disclosed an elongated sella without much depression of its floor and with the dorsum strongly marked, definitely abnormal, but of an uncommon pattern. The optic foramen in special views caused some comment

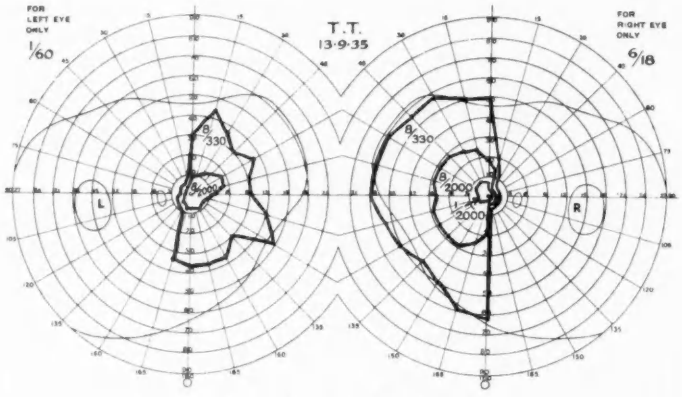

FIG. 16.—Visual fields of Case 11.

at the time, for although the right was normal, the left had an exceptional thinning of its lower and outer margin. This is not in itself very uncommon in old-standing pituitary enlargements, according to my own observation, but in

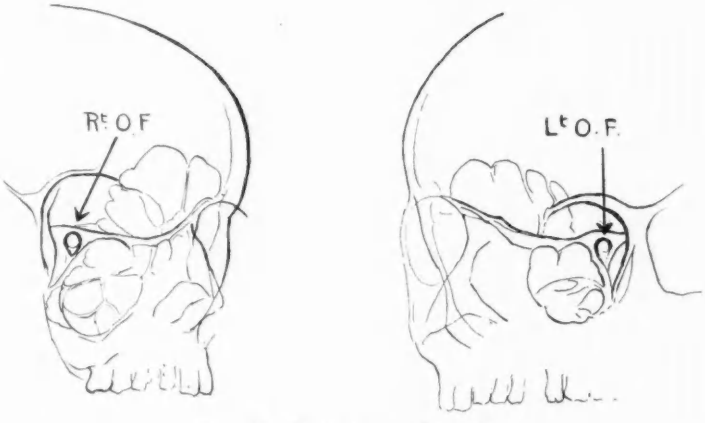

FIG. 17.—Optic foramen (Case 11).

this particular case there was an additional peculiarity. There was a definite enlargement of the inner end of the sphenoidal fissure, not, to be sure, of quite the exceptional quality presented in Case 5, but none the less reminiscent of

it (fig. 17). This was unusual with a pituitary adenoma, but it was not thought to be definite enough to be completely diagnostic of aneurysm.

Operation.—September 13, 1935. Left frontal osteoplastic flap (the side of worse vision). Extradural elevation of left frontal lobe. When the left optic nerve was brought into view it was seen to be coloured yellow and there was brownish staining in the arachnoid to its inner side. On dissecting the nerve free from its arachnoid covering a brownish tough-walled tumour with contents of putty-like consistence was seen filling the sella, but its anterior edge fell a little short of tuberculum sellæ. The surface of the tumour was curiously opaque, and as a better view was obtained it was seen to pulsate. A finger introduced to verify this fact confirmed strong pulsation in the tumour. It was possible that this was transmitted from the carotid vessels in the cavernous sinus, though this would be unusual, but it was very important to make as sure as possible that the tumour was what it appeared to be, an aneurysm and

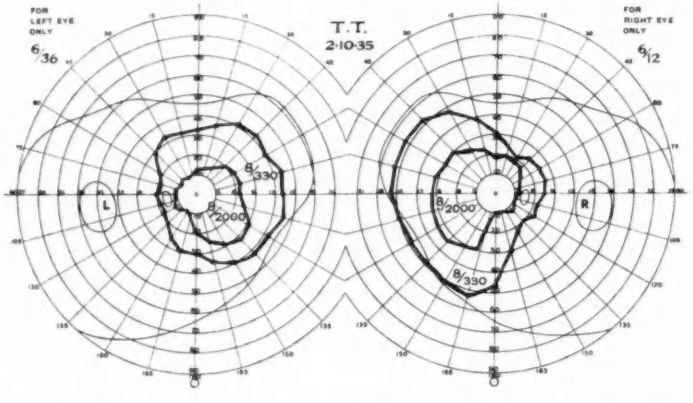

FIG. 18.—Visual fields (Case 11), two and a half weeks after tying left internal carotid artery.

not an adenoma. A hollow needle was therefore introduced into the tumour and a little blood withdrawn. On removing the needle a smart hæmorrhage occurred, which was quickly arrested. A second puncture further back led to withdrawal of blood easily in the syringe, and the removal of the needle this time was followed by considerable bleeding. Cotton pledgets held in position for a few minutes completely arrested the hæmorrhage; a muscle graft was substituted. It was now as certain as it was possible to be that this was an aneurysm, but there was nothing in its appearance to suggest from which vessel it had come. It was infra-chiasmal and probably represented a blow-out from the carotid as it pierced the dura beneath the left optic nerve, the side on which vision had first been affected. The thinning of the lower wall of the left optic foramen in the oblique radiogram of the orbit supported this

view. He had bled so smartly on puncture that I feared to leave him without ligature. After closing the frontal wound the left internal carotid was tied in the neck. Recovery was uneventful. There was no hint of weakness of the right hand or of aphasia; dynamometer readings ranged around 140 to 160 kilos during the week after operation. There was a very definite and worth-while improvement in vision, following arterial ligation, acuity going up in the left eye from $\frac{1}{60}$ to $\frac{6}{36}$ and in the right from $\frac{6}{18}$ to $\frac{6}{12}$ three weeks afterwards. The improvement in the fields is shown in the charts (fig. 18).

This patient writes in September, 1937, to say that he is very well indeed and cycles ten miles a day to his work.

Comment.—In this case field defects quite indistinguishable from those of pituitary adenoma were present. The history was short, eight months in all, but there was nothing dramatic in the manner of onset. The bodily configuration suggested pituitary dysfunction, hypopituitarism, though the cause might well be pituitary compression from any cause. The sella was curious, it was elongated forwards rather than excavated downwards. The peculiarity of the view of the left optic canal has already been alluded to and especially the opening up of the sphenoidal (superior orbital) fissure.

Case 12.—E. W., female, married, aged 44, was admitted to the Neuro-Surgical Service of the Manchester Royal Infirmary, January 13, 1937, complaining of double vision and failing vision in the right eye. She was quite well, apart from unexplained amenorrhœa dating back over eight years, until May, 1936. One morning she awoke with nagging pain over the right forehead. Within forty-eight hours the pain had become very severe indeed, shooting up over the right side of her head and preventing her from sleeping. It continued thus for two weeks and gradually abated, but did not leave her for another month. On the third day of this illness she had diplopia and was admitted to a Sheffield Hospital on this account. It persisted for four months, and since then she has only observed it on looking upwards. She wore an eyeshade over the right eye for four months and on removing it she discovered that vision of the right eye was affected. When reading she found that, with the left eye closed, the print in the temporal field of the right eye was blurred. She was admitted to the Sheffield Royal Infirmary under Dr. Gurney Yates, who found a suggestive bitemporal field defect and made the diagnosis of carotid aneurysm compressing the chiasma. He referred the case to the writer. On examination her build was not remarkable in any way, rather spare, her skin lacking the smoothness and pallor of hypopituitarism. There was right-sided hyposmia, left normal. Pallor of the right optic nerve head, left normal. V.A.R. $\frac{6}{60}$, V.A.L. $\frac{6}{9}$. Visual fields showed an upper temporal quadrantic defect to a 6 mm., a complete hemianopia to a 1 mm., white object on the tangent screen, right eye. The left field showed an upper temporal quadrant only to the 1 mm. white disc, to larger discs the field was full (*see* fig. 19).

There was slight paresis of the left superior rectus, but no other defect of ocular movement could be observed. The right abducens was slightly weak; apparently at one time she had a frank paralysis of this external rectus and wore the eye shade on that account. She was now only troubled by diplopia on looking upwards, left image below right. No anæsthesia of either trigeminal could be detected, though it was carefully searched for on several occasions in view of the distribution of her sudden early pain, so suggestive of aneurysm. Corneal sensation equal and normal. The remaining cranial nerves were normal. No abnormal neurological signs were detected in the arms or legs. Wassermann reaction negative. Cerebrospinal fluid—pressure 80 mm., albumin 35 mgm., globulin normal, cells less than one, Lange curve normal. Basal metabolic rate +1. Sugar tolerance curve normal. X-ray showed an enlarged sella strongly suggestive of an intrinsic pituitary adenoma and without porosis of the clinoids.

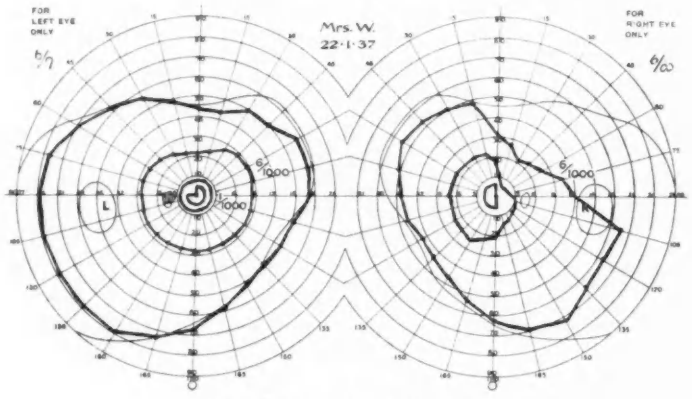

FIG. 19.—Visual fields (Case 12).

In view of the six-year history of amenorrhœa, the bilateral oculomotor disturbance, and the uniform sellar enlargement there was much to be said for a chromophobe adenoma as the cause of her troubles. On the other hand, the suddenness of the onset, the extremely severe pain at its commencement, and the presence of ocular palsies of any kind (though they do occur, if rarely, with pituitary adenoma) spoke for aneurysm. The question was undecided until operation, which proved that Dr. Gurney Yates' diagnosis was correct. On January 26, 1937, a right frontal osteoplastic flap was turned down under avertin and gas anæsthesia. Entrance very difficult owing to exceptional dural adhesions. An intradural approach was made to the right optic nerve. This presented a curious appearance, for it was looped upwards and outwards by a rounded structure, covered with dura, beneath it. Towards the left the diaphragma sellæ, which was not much elevated, sloped away sharply, so that

the left nerve was only slightly compressed (fig. 20). A small incision was made into the pituitary diaphragm, which was very thick. No tumour escaped, and cautious examination disclosed an encapsulated mass not much larger than a cherry occupying the right half of the sella. There was no detectable pulsation. A lumbar puncture needle was inserted into the swelling to the inner side of the right optic nerve. Considerable pressure was needed to puncture it, when the needle filled with blood. Several small syringefuls were withdrawn in order to establish the fact that the cavity was truly aneurysmal and was not a blood-filled cyst without communication with a vessel. On removing the needle there was no bleeding but a small piece

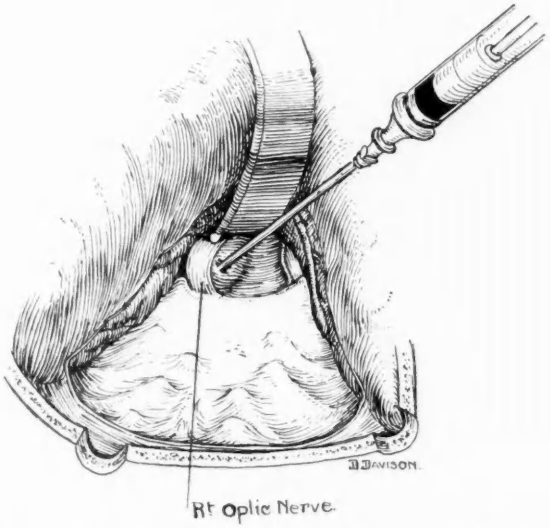

FIG. 20.—Case 12. Operation sketch of aneurysm compressing right optic nerve.

of temporal muscle was plugged into the opening in the diaphragma for security. Usual closure with a temporary drain. Convalescence proceeded smoothly but for the development of an isolated generalized convulsion on the eighth post-operative day, probably due to œdema, as two anterior parasagittal veins had had to be coagulated. There was no repetition of this fit, and she left the Hospital on the fifteenth post-operative day with her essential condition unchanged.

Comment.—The diagnostic problems have already been discussed. It is to be presumed that her amenorrhœa was of pituitary origin. She must have had a small aneurysm compressing the gland for some years prior to the final blow-out. The formation of the larger aneurysmal

sac can be very accurately dated to a time only seven months prior to the exposure of the aneurysm. The treatment of this case cannot be said to be completed. She will compress the right carotid for fifteen minutes two or three times daily with the object of inducing thrombosis and opening up a collateral circulation. If the cavity and field restriction in the right eye continue to fail, and especially if there is any further encroachment of the left field, then the right internal carotid must be tied. The aneurysm had been demonstrated to have a thick wall and is covered also by dura so that there is no immediate necessity for ligature. Nine months later this patient continues to be well with no further change in vision.

Previously Recorded Cases.

I have been able to find records of only sixty-six examples of disturbances of vision by aneurysm in the literature, additional to the twelve just described. They are set out in a synoptic table at the end of this paper. This takes no account, as it might have done, of visual loss, as described by Leslie Paton, from subhyaloid hæmorrhage in diffuse subarachnoid bleeding. But as the mechanism of the production of amblyopia and scotoma formation is quite different in this state from that in the pressure affections of the optic pathways proper, I have omitted my own examples and those of others. It is to be remembered, none the less, as a clinical point, that sudden blindness, or blurring of macular vision, may be due to effused blood in the optic sheaths and diffuse subretinal swelling, rather than to sudden chiasmal compression. The case of J. Hutchinson, Sen., once much quoted, appears to have been of this type, whilst in that of J. Hutchinson, Jun., the same agent may have been effective, but there is also necropsy evidence of chiasmal compression. I have numbered the latter's case amongst those tabulated, but not the former's. In the case of Wildbrand and Saenger, and in that of Van Bogaert, Helsmoortel and Nyssen, the sudden blindness was caused by chiasmal compression, and these cases are naturally included.

Study of the literature brings interesting reflections on the increasing part which retinal and visual-field studies play in diagnosis. The older writers were content to comment to the best of their ability on the sight of their patients, but their accounts are, by modern standards, woefully lacking in precision. Thus it is only during the last quarter of a century that the searcher can find the kind of information which he requires, if he wishes to obtain confirmation elsewhere for personal

observation, to reinforce his own findings by similar experience in the hands of others. There must have been important visual disturbances, capable in modern times of informative analysis, in cases which have had to be omitted, by reason of their vagueness, from the analytical table at the end of this paper. Such was Sir Gilbert Blane's case in 1791. This was the first English record of an intracranial aneurysm. His patient was suddenly seized with dimness of vision and suffered from recurrent maniacal attacks for some years. The post-mortem was historic, for it was conducted by John Hunter, Holme and Jenner, who found bilateral aneurysms of the internal carotid trunks an extremely rare condition. Cases are referred to in similar terms by Patterson [61], Bristowe [12], Coe [15], Chevalier [14], Smith [74], Delpech [22], Gull [39], Humble [45], Wood [90], and Timothy Holmes [44]. In a few others, such as Spurgin's [76], Peacock's [62], and Squire's [77], compression of the chiasma or optic tract was noted at necropsy, but no mention is made of clinical tests for vision. Spurgin's case is particularly noteworthy, for, writing in 1825, he describes the case of a man aged 55 who suffered for a short time from fits. He remarks that the patient had cataracts, but could distinguish light from darkness with the right eye. At post-mortem an aneurysm, the size of a hazel nut, of the right anterior cerebral artery was found immediately to the outer side of the olfactory nerve and pressing on the right optic nerve. He removed the right eye and found its dural sheath thickened and distended with blood. This is probably the earliest reference to the presence of blood in the optic sheath in subarachnoid hæmorrhage, and it was made by a country practitioner. An important contribution was made by Lebert [51] in his series of letters to the *Berliner klinische Wochenschrift*, an admirable review of intracranial aneurysms up to 1866. He states that unilateral blindness is a common result of these lesions, but does not discuss the matter in any detail or furnish any personal observations.

Considering the quantity of the literature on aneurysms, the number of cases relevant to the present discussion is not large, but there have been many disappointments. For example, Beadle's great collection of 555 aneurysmal histories and specimens includes 114 new cases or specimens, but his paper is remarkably free from details of the symptomatology of the aneurysm, although the general effect of his paper is impressive. One case only, that recounted to him by Nettleship, has been gleaned from his remarkable series as having a bearing on the present subject. A good deal of his personal material came from

asylums, as did two of Byrom Bramwell's, a vague but important clinical fact. In Fearnside's important paper on aneurysm, his Case 23 had lost the vision in the right eye, but he had had an iridectomy and the eyeball is spoken of as shrunken. At post-mortem the optic nerve was found grey and atrophic, but its precise relation to an aneurysm at the junction of the right anterior cerebral and anterior communicating arteries is not mentioned. Two cases were found in Schmidt's valuable paper on the material from the Commune Hospital, Copenhagen. The more recent case of Demay, Bertrand and Perisson [24] must be omitted for lack of accurate record. In this case a young woman aged 32 complained of failing vision, and later became maniacal. A large carotid aneurysm was found at post-mortem, reducing the chiasma and optic tracts to narrow bands. The authors frankly regret the omission of more detailed clinical notes on her vision.

Foster Moore has illustrated an admirable example of intracranial aneurysm of the ophthalmic artery, an extremely rare condition. This occurred in a man aged 35, who suffered from rheumatic endocarditis, and caused sudden blindness in the right eye. At post-mortem two months later the right optic nerve was found divided by an aneurysm of which he publishes an excellent coloured drawing [55]. Dempsey [23] and Schmidt [69] record other examples. Recently Sandford, Craig and Wagener have recorded a curious case with an altitudinal hemianopia due to aneurysmal dilatation of a cirsoid type in both ophthalmic arteries. Vision was greatly improved by cutting away the roofs of the optic canals to decompress the nerves.

The writer has omitted visual defects in arteriovenous (fistulous) cavernous aneurysms because the problem in that type is usually, but not always, different. There is never any difficulty in diagnosis, and such visual disturbances as occur are often of a kind beyond the scope of the present paper. For that reason Dandy's recent cases, Schmidt-Rimpler's and Dempsey's, amongst others, have been excluded. It may be added that an aneurysm of a saccular type often is present, even if it is fistulous, and it would be interesting sometime to evaluate the visual defects in such of these cases (and they are many) as are non-traumatic. The last condition is added because an optic nerve can be injured at the same moment that the skull is fractured.

Comments on the Series.

Age-sex.—There is in my own cases a marked disproportion of the sexes, the majority being females (nine out twelve). In another series

(Group 3) of sixteen saccular aneurysms in the cavernous portion of the carotid all were females save one. In the series collected from the literature the discrepancy is not so great (F. 35, M. 31). Peculiar female vulnerability to cerebral aneurysm has been noted by Fearnsides and by Schmidt and seems to be a fact, in distinction to the acquired and often syphilitic aneurysms elsewhere in the arterial tree, which occur most often in males. As for age, most of those which have evolved in a neoplastic manner, relatively slowly, have occurred in patients over 30. But Foerster's case was 20, Schmidt's case 20, Packard's 21, Dempsey's 22, Conway's 23, and one of my own 23 (Case 11). The writings of Fearnsides, of Symonds and others, and our own experience, has familiarized us with the fact that congenital aneurysms may occur at all ages and that they are naturally common in youth. The pathology of the type of aneurysms under discussion seems in no way to differ from that of the so-called "berry" aneurysm, so well investigated by Eppinger [28], Wiley Forbus [33], by Drennan [26] and by Tuthill [84]. They mostly occur like other aneurysms, at the bifurcation of a large vessel, in this case the internal carotid, perhaps where the ophthalmic artery leaves it or, in the suprachiasmal group, at the point where the anterior cerebrals are joined by the anterior communicating.

Symptomatology.

Some years ago it was a very generally accepted view that the diagnosis of an intracranial aneurysm presented a well-nigh insoluble problem. That this is no longer true is due to several developments, of which one of the most important has been the better understanding of tumour symptomatology, taking into account not only the situation of the lesion, but its pathology. It can be well understood that aneurysms must have been difficult to diagnose at a date when intracranial tumours were imperfectly understood, for the clinician could have had no safe starting point in his approach to the problem. At the present day we are better armed in our knowledge of the evolution of the tumour groups, and we have new weapons in X-rays and angiography which can often act in a decisive manner. On the whole the differentiation of aneurysms from other lesions which can interfere with vision centres around the pituitary adenomas and suprasellar tumours, and this immediately brings us to a consideration not only of the visual fields and X-ray appearances, but of certain other co-existent states, either of an endocrinal or neighbourhood type, which are common in one but

not in the other. It must be borne in mind that the fields are to be linked with atrophic discs. A homonymous field defect with papillœdema is a neurological commonplace; the case is far otherwise when the nerve heads are atrophic. At the last analysis the differential diagnosis of a chiasmal lesion rests on the following points:—

(1) The nature of the field defect, coupled with the manner of its evolution (a point on which it is unusual to be able to gather detailed information) and the rapidity of its development.

(2) The degree of pain associated with the evolution of the visual defect.

(3) The co-existence of other neurological signs.

(4) The presence or absence of tuberal or endocrinal disturbance.

(5) The X-ray evidence.

Each one of these requires comment.

Visual Fields.

A study of the recorded cases brings to light one very important thing, the varying nature and pattern of the visual defects in the same patient at different times. For instance in Harris' case there was first blindness in both eyes with recovery; then a left central scotoma, then a right temporal hemianopia with a tendency to, but no certainty of, a right homonymous defect. Post-mortem findings made it certain that the homonymous defect was correct. Much the same fluctuations were present in Case 7 above, Foerster's case, and in Conway's. Conway's paper on his case indeed will repay careful study, for he includes diagrams of the visual fields taken on six occasions over a period of nine months showing wide variations in a bitemporal hemianopic defect, with remarkable spontaneous improvement continuing up to three days before his sudden death. Difficulties such as these impede the giving of a clear-cut analysis of the exact pattern of the visual loss in all the cases. With one eye blind and a temporal defect in the other it is always difficult to tell whether the field loss was basically bitemporal or homonymous, but the reader who runs his eye down the very abbreviated case histories in the synoptic tables will rapidly get an impression of the types that the cases have exhibited.

If the collected cases and the writer's own, 77 in all, are analysed the results are: (1) Bilateral amaurosis, 7 cases; (2) monocular central scotoma, amblyopia, or blindness, 25 cases; (3) the same, combined with temporal hemianopia in the contralateral eye, 10 cases; (4) homony-

mous hemianopia, 11 cases; (5) bitemporal hemianopia, 15 cases; (6) varia, examples in which analysis is difficult or not covered by the foregoing descriptions, 9 cases. The manner in which these variations of visual defect are brought about is worthy of inquiry. The section on complete blindness need not detain us very long (cases of temporary amaurosis from subhyaloid exudate are omitted). The writer's own case was curious and not without ambiguity, moreover the late history is unknown. In others the blindness was of sudden onset and chiasmal pressure authenticated by post-mortem dissection. The most important and largest combined groups are the second and third, monocular blindness with or without a temporal field defect in the other eye 33 cases.

It has already been stated that the commonest aneurysms to cause visual disturbance are those of the internal carotid. These may be supraclinoid or infraclinoid (cavernous) in position. It is strange that the latter which so often occur as a massive, saccular or fusiform non-fistulous type occupying the cavernous sinus should so rarely cause any defect of vision. The sac at necropsy may be in contact with the optic nerve, yet there has been no recognizable field defect. Recently McKinney, Achree, and Solz [54] have published four cases of this type with the usual associated paralysis of the nerves in the wall of the sinus (cavernous syndrome of Foix) and in these there has been a monocular upper nasal quadrantic loss. Packard and Zabriskie had a similar experience. Usually the lower and outer wall of the optic canal will be found to have been eroded in such cases. A more recent and admirable example is that of de Vet and Zeckel, which concerned a young man with total ophthalmoplegia, partial anæsthesia of the face, and blindness in the homolateral eye. In contrast with this group the aneurysm which springs from the supraclinoid part of the artery causes pressure on the optic apparatus which is certain, and usually immediate, in its effects. The pattern of the visual loss is by no means uniform.

Monocular amblyopia.—In the recorded cases the character of the monocular defect varies from dimness of vision, through various scotoma types, to blindness in the ipsilateral eye. It is probably very difficult for an aneurysm to remain so small that it compresses either the optic nerve, the chiasmal junction, or the tract alone, if it has sprung from the internal carotid artery. Sooner or later it is bound to compress two at least of these three components, and often all three. The post-mortem records often refer to pressure, not only on the optic nerve but on the tract and chiasma as well. The character of the field defect that results from an indentation of the outer edge of the chiasma is a very

interesting subject for discussion and further study. Unfortunately very few fields have been examined by quantitative perimetry and there is very little information to be gleaned from the collected cases that would illustrate the unique compression which a carotid aneurysm can exert.

When the aneurysm has arisen from the internal carotid the field defects should be characteristic and allied to Traquair's "junction scotoma." The outer side of the angle of junction between the optic nerve and tract at the chiasma is one which no other lesion but an aneurysm can easily occupy. Now, the crossed fibres in the chiasma which form the knee, or loop, of Wildbrand and Saenger come sufficiently far across to be damaged by an indentation at that point, and thus arises the field picture which experience will probably show to be most characteristic of internal carotid supraclinoid aneurysms—a scotomatous or rapidly failing ipsilateral eye with a definitely homonymous hemianopic overlay in the fields of both eyes. If Wildbrand and Saenger are correct (they are confirmed by Balado) in their plan of the crossed fibres in the chiasma then the temporal defect in the opposite eye should be chiefly in the upper quadrant. The temporal field defect in the opposite eye may be more extensive than this by the time that the case comes first to skilled notice. For the aneurysm may extend chiefly backwards under the optic tract behind the chiasma, producing, of course, a congruous homonymous defect. But as a rule it will compress the junction of the ipsilateral optic nerve with the chiasma as well, so that it will be depressed acuity of the eye on the side of the aneurysm which excites comment and stimulates investigation. Some good examples will be found in Table III.

Central scotomata are by no means uncommon with pituitary adenomas, which arise medially, and should produce a well-equalized pressure effect in the prechiasmal space, but often do not do so. The capsule has a tendency to give way in an eccentric manner so that a nubbin of tumour breaks through under one optic nerve, stretching the nerve over it. In this way a central scotoma must develop. The basic field deficiency is, however, bitemporal, and the absence of pain, so rare a feature of the chromophobe adenomas, helps further to differentiate the cause.

Bitemporal hemianopia.—The production of a bitemporal field defect by a supraclinoid aneurysm is rarer (*see* Table V of collected cases). The defect may be produced by herniations of either the internal carotid the anterior cerebral, rarely the middle cerebral. When the aneurysm comes from the carotid it must break through the inner wall of the

cavernous sinus, or arising at the origin of the ophthalmic artery pass medially under the optic nerve into the sella. Its enlargement there will produce a picture like that of an adenoma, with enlargement of the sella and possibly amenorrhœa (as in Case 12). But the fact that the aneurysm must always belong more properly to one side than the other leads to much greater loss of acuity on the one side. Thus it comes about that monocular scotomas may be associated not only with a homonymous defect, but also with a bitemporal. This happens frequently enough in pituitary adenomas and a differential diagnosis from the fields may not be possible. It is in these cases that the suddenness of onset of the malady, the pain accompanying it, and perhaps the occurrence of oculomotor palsies too, help in differentiation. The time factor becomes a most important one in differential diagnosis, and if it is not more stressed here it is because the case histories which have gone before emphasize the matter strongly enough. It may be noted that a sudden hæmorrhage into a pituitary tumour causes symptoms so like those of an intra- or parasellar aneurysm that differentiation may actually be impossible, unless acromegaly be present.

Bitemporal hemianopia produced by aneurysm of the anterior cerebral may eventually have nothing in its form to denote its cause, but in the early stages the loss is in the inferior temporal fields, rather than the superior as in pituitary adenomas. Such a finding is characteristeric (*see* Cases 7 and 9) and can scarcely be mimicked by indentation of the dorsum of the chiasma by normal, but stretched, anterior cerebrals with a massive pituitary tumour below. Later, when the bitemporal hemianopia is fully developed we must depend on the ancillary diagnostic points already outlined.

Homonymous hemianopia.—A few cases of homonymous hemianopia are to be found in Table III, those which have already been discussed as complicated by an additional defect in the eye on the side of the aneurysm, others are given in Table IV. Curiously enough the defect was only once produced by an aneurysm of the posterior cerebral artery. Usually it arose from the carotid or from the middle cerebral or even from the anterior cerebral; the last seems strange. Reference to fig. 1 will show, however, that it is quite possible for an aneurysm arising in any part of the Circle of Willis to reach and compress tractus opticus quite easily, insinuating itself backwards and outwards either above or below the chiasma.

It can be concluded that the most characteristic fields of aneurysms (the fundi being normal or atrophic) are therefore: (*a*) A scotomatous

homolateral eye, with an overlying homonymous defect in the nasal field of that eye and in the temporal field of the other; (*b*) bitemporal defects, only clearly aneurysmal because of inferior quadrantic loss as the earliest sign, or because of the suddenness of development, or because of ocular muscle palsies, as well as pain; (*c*) nasal hemianopia in the ipsilateral eye.

Other Neurological Symptoms and Signs.

Pain and headache.—Pain is a far more frequent accompaniment of aneurysms than of pituitary adenomas. It is not rare for the latter to progress to severe chiasmal compression and blindness without the patient suffering any noteworthy pain at all. This is certainly true of the chromophobe adenomas. The alpha-granule type of acromegaly is often an exception to this rule, but it is by no means sure, even in these cases, that the pain is due to sellar expansion. In many cases the pain seems to be due to tensile changes in the bone, for whilst the acromegalic patient may, and often does, complain of severe headache, he has much the same pain in his back and limbs. On the other hand, the aneurysmal subject has pain of very great severity, often agonizing in degree, and of abrupt onset. In many cases the pain is local in the forehead, or at least it is unilateral. This pain may be accompanied by local numbness in the forehead (in Cases 4 and 5 it was general over one trigeminal field) and if this is abrupt in its origin diagnosis is immediate and certain. The characteristic anæsthesia of the ophthalmic division of the 5th nerve, so striking a feature of the subclinoid aneurysm, which does not usually compress the chiasma or optic nerve, does not occur in supraclinoid aneurysms which affect vision more frequently. Severe pain in some form or another, appearing suddenly, and roughly contemporaneously with a disturbance of vision, must always strongly suggest aneurysm.

Hemiparesis.—Weakness of the limbs of a transitory kind, numbness or tingling in the hands or feet, are rare accompaniments of aneurysm. Hemiparesis occurred in two of the cases in this series and will be found to have been present, occasionally only, amongst the collected cases.

Mental changes.—The high incidence of aneurysms, especially of massive type, at necropsies in asylums must have a meaning. This is surely not that the insane are particularly liable to develop aneurysms, but that aneurysms can often lead to insanity. In the writer's own series there have been two cases in which at the time when first seen mental deterioration was the outstanding feature. One was Case 5,

the other, a woman aged 50, not included in this series, with unmistakable signs of infraclinoid carotid aneurysm of eight months duration, and mental disturbance developing almost immediately after the ocular palsies and pain which heralded the formation of the aneurysm. Some form of mental derangement was not uncommonly present in the cases collected from the literature, notably in the examples of Byrom Bramwell, and of course, Beadles. It seems likely that it is circulatory failure, rather than the pressure of aneurysmal mass, which causes these alterations in behaviour and character which are apt to make the patient a fit subject for segregation in an asylum.

Oculomotor palsies.—Ophthalmoplegia, either total or incomplete, is the characteristic picture produced by aneurysms of that part of the carotid artery which lies in the cavernous sinus (i.e., in its sub-clinoid portion). As has been said, it is only rarely that this particular aneurysm produces any defect of vision. In Cases 4 and 5 in the present series ptosis from 3rd nerve palsy was present, and diplopia was an early feature in Case 12. It may be said that any case in which severe pain in the head is followed by diplopia there will always be a strong suspicion that an aneurysm had produced it. This would be more likely still if the pain was specially referred unilaterally to the forehead and the diagnosis would be certain if hypoæsthesia or numbness rapidly developed. Of course diplopia after headache is a common feature of raised intracranial pressure. It is the quality of the pain, and the rapidity of appearances of the ocular palsy, which distinguishes the aneurysmal cases. Abducens palsy in association with evidence of chiasmal compression is commoner with aneurysm than with pituitary adenomas, for the nerve is insulated from the sella by the carotid artery, on the outer surface of which vessel it lies. A good example was Case 10. The writer has seen three cases of pituitary adenoma with oculomotor paralysis, and it is indeed curious that a frank lesion of the motor nerves to the eyeball is not a commoner feature of pituitary tumours. In actual fact diplopia is not infrequent with them, but the buffering of the nerves by the carotid artery saves them from direct and obvious paralysis.

Anosmia.—This ought to be a common symptom in aneurysm, but it is almost always absent, though uncinate attacks are not uncommon (Case 8), as would be probable with a tumour so close to the uncus. Anosmia is only produced by lesions which compress the olfactory bulbs, the nerve itself stands displacement and light compression very well.

Tuberal signs.—Somnolence, sweating, visceral disturbance, tempera-

ture variations, cardiac rate and rhythm variations are all too recent tuberal or hypothalamic signs to have produced instructive comments in the literature of aneurysms. In the series recorded above nothing was noted but change of water balance in two cases, but in neither was it striking. Polyuria and polydipsia is mentioned by Van Bogaert *et al.*, and by Lodge *et al.* No doubt much more information on these points will come in future. But it is unlikely that hypothalamic signs will occur in any great degree because it requires an invasive, destructive lesion of tuberal centres or pathways to induce them. In a fairly large experience of third ventricle lesions the writer has been impressed by the absence of autonomic signs if the tumour or cyst merely indents or presses on the neighbourhood structures without cutting into them.

Dyspituitarism.—The basal metabolic rates are given above in some of my own cases. In only one (Case 11) was there any notable change, a decrease suggestive of hypopituitarism. This patient and another male (Case 9) had the slightly yellowish skin suggestive of a pituitary adenoma. The question of amenorrhœa next arises, and in only one case (Case 12) did it introduce serious doubt in the interpretation of the cause of the visual defects and in general as to her malady. Unless the aneurysm fills the sella turcica and severely compresses the pituitary, as it did in Cases 5, 7, 10 and 12 of the females, no change in menstrual periodicity is likely. It so happens that only in Case 12 was the patient of such an age that the history of an eight year amenorrhœa could be held to be significant. This, then, is at first sight an important differential point, but given a pituitary adenoma in a female at or beyond menopausal age and it is clear that reliance must be placed on other things, such as the occurrence of severe, or even agonizing, pain at the beginning of the visual troubles and that no important conclusion can be arrived at from a consideration of endocrinal disturbances alone.

The X-ray appearances.—These must be grouped under two headings: (*a*) Opacity in the wall of the aneurysm; (*b*) alterations in the bones of the base of the skull.

(*a*) *Opacities in the wall of the aneurysm.*—The loss of the muscular coat and elastic fibres, the characteristic change in the aneurysmal walls with the conversion of the vessel into a fibrous sac, is accompanied frequently by the deposit of calcium salts. Such patches of calcification could be seen in the radiographs of Cases 5, 9 and 10. Although many aneurysms, when they have reached this stage, stabilize and grow slowly, they are none the less capable of further expansion at some point. I have, on the other hand, followed a case for fourteen years and seen

little change in the aneurysm on periodical X-ray examinations. In Case 9 above there has been an increase in symptoms, although there is a shell of well-calcified wall in the greater part of its extent. The calcification can, by the nature of the communication of the sac with the great vessel, never be complete, and there will be weak places at the neck of the sac. It is well known, similarly, that however well an aneurysm may be filled with clot, it yet may rupture at that part where it is still filled with circulating blood, as happened in Case 8. The fine line of calcification seen in X-ray pictures is unlike that of any other intracranial lesion. When seen as more or less complete circles, they have been called, for no very good reason, "Albl's rings." It is the density and narrowness of the line which is diagnostic. Occasionally small plaques of calcification can be seen in the walls of the vessel within the larger circle, and difficulties can then arise as to whether we are faced with a cyst of the pituitary anlage or teratoma. In the latter the calcification is generally more irregular, and rarely so high in the cranium. There are cases, however, in which there will be difficulty in interpretation, others will be simple. The calcification seen in gliomas, epidermoids, and in dural exotheliomas can never cause any difficulty in differentiation.

(*b*) *Alterations in the skull.*—Destruction of the sella turcica is the most frequent and most obvious effect of carotid aneurysms. The sellar patterns in the present series of cases confirms the fact that though the alteration can closely simulate that of the pituitary adenoma, more often it is not likely to cause confusion. The tendency is towards lateral erosion of the sella and damage to the anterior clinoids, especially that of the same side, a point not always easily established unless special care is taken to demonstrate the clinoid processes. Aneurysms of the anterior end of the carotid have a particular tendency to widen the sphenoidal fissure, a feature illustrated by three of these cases. This enlargement can be seen in the ordinary anteroposterior views, but it is particularly well demonstrated by oblique views of the orbit showing up the optic canals. The writer has referred to this elsewhere [47]. In this tangential view another feature is visible, erosion of the lower and outer wall of the optic canal, a point which Twining and the writer have come to regard as almost, if not quite, pathognomonic. The internal carotid curves forwards to the back of the sphenoidal fissure, and upwards to the inner side of the anterior clinoid process. A blow-out in this situation will damage both in course of time, it will porose the strut of bone which passes from the side of the body of the sphenoid

to the lesser wing to complete the optic foramen below. The only other lesion likely to damage this bridge of bone would be a dural exothelioma arising from the back of the wing of the sphenoid and floor of the temporal fossa anteriorly. There is one such case amongst my recent material, but there was loss of all the structure in the sphenoidal wing, a general blurring, not likely to be mistaken for an aneurysm, whilst the optic foramen had in that case disappeared altogether.

It would be impossible to stress too heavily the help which these auxiliary aids to diagnosis can give. There is no other way of knowing what is the state of the sphenoid and optic canal, information which must be correlated with the clinical history and findings for the making of a correct diagnosis, except by taking special oblique X-ray views.

Angiography.—In no cases can Moniz's method of angiography be of greater service. Angiography has become a well-accepted diagnostic aid and when the results are positive the solution of what may have been a clinical puzzle is certain. It is important to recognize that it may fail, either through faults in technique or through an aneurysm having too small a cavity to throw a clearly distinguishable shadow amongst a maze of branches. The best pictures are given by saccular aneurysms in direct communication with the internal carotid itself and are less certain if it springs from a subsidiary vessel. The advantage of angiography is obvious, for it does away with the need for what might be a hazardous exploration and tells us more definitely than any other method from precisely which artery the aneurysm has arisen, thus giving a definite lead to vessel ligature, if that should be thought desirable. The actual size of the scour or tuft of thorotrast seen in the aneurysm may be disappointingly small, but it will usually be of sufficient size to be unmistakable. The writer has not used angiography in all his cases because he is not yet entirely convinced that it is a completely harmless procedure.

Treatment.

I feel more and more convinced that there is only one useful treatment for these cases, and that is carotid ligature. The cases recorded in this paper do not show much evidence of this belief, for the carotid was tied only in Case 11. However they must be regarded as an attempt to clarify the clinical picture of aneurysm, an exercise through which treatment has emerged. Without going into the operative question in great detail, one or two broad principles can be laid down. Ligature has been the treatment for aneurysm since the days of John

Hunter. The treatment might therefore be applied to these particular aneurysms without equivocation, without reservation, if it were certain that tying the carotid would do no harm. Allowing for the fact that the dangers of carotid ligature have been exaggerated, there is no doubt that there are risks, nor is there any absolutely sure way in which they can be avoided. This being so, only those cases will be operated upon where progressive failure of vision, or where persistent and wearying pain, make intervention imperative. And even in these, the carotid will only be tied if it can be proved that digital compression for half an hour is tolerated without ill-effect. Furthermore, when the operation is undertaken, the final ligature will not be applied until the effects of a temporary one have been observed for a full hour (local anæsthesia is a *sine qua non*). By such means as these the majority of disasters ought to be avoidable. I have tied the internal carotid nine times and the common carotid twice. In one case only was there any anxiety, on account of a temporary aphasia, which cleared up later. Clearly carotid ligature is of no use for aneurysms far removed from the main trunk. Some of the more accessible ones may come very occasionally to be excised. Tönnis has already removed a small aneurysm of the anterior cerebral artery. Dott has packed muscle round one, whilst the writer has also packed one with muscle and partly cut it away (an anterior cerebral aneurysm burrowing into the right frontal lobe and not affecting vision). In the end each case will be treated on its own particular merit.

Summary.

(1) Twelve cases of intracranial aneurysms affecting the visual pathways are reported out of a personal series of fifty-three aneurysms.

(2) Sixty-six previously recorded cases are analysed.

(3) The present series is compared with the writer's other aneurysmal material.

(4) The twelve cases are divided into four groups according as they interfere with the visual cortex, those that compress the optic tract, the chiasma, and the optic nerves.

(5) The field defects in these lesions are fully discussed and certain characteristics emphasized either in pattern or manner of development.

ANALYSIS OF RECORDED CASES.

I.—Blindness (7 Cases).

Author	Sex	Age	Visual defect	Other clinical findings	Site of aneurysm
Stilling 1833	F.	42	Sudden blindness; later P.L. in L. eye. Mydriasis	Fell unconscious; recovered in an hour. Died in 24 hours	R. int. carotid, size of walnut, compressing chiasma and tuber
Ogle 1865	M.	—	Blind 4 years	Paraplegic 12 years. Imbecile lately	Small aneurysm L. anterior cerebral, compressing L. optic tract
Hanot 1872	F.	50	Blind L. eye 8 years. Blind R. eye 2 years.	Deafness 10 years. Fits 8 years. Intelligence impaired. 18 months; later deaf, blind and imbecile	Aneurysm 5 × 3 cm. L. cerebral, compressing chiasma and both optic nerves. It was embedded in the 3rd ventricle
Hutchinson, J., jun. 1889	M.	20	Sudden loss of sight. Hæmorrhage into retina	Paresis R. arm and leg	Aneurysm of basilar artery compressing chiasma from behind
Wildbrand and Saenger 1915	M.	55	Sudden blindness. Fundi normal	W.R. +. Survived 6 days	Chiasma flattened and compressed by aneurysm of L. internal carotid
Van Bogaert, Helsmoortel and Nyssen 1929	M.	37	Sudden blindness L. eye 8 days; later R. eye. Bilateral papilloedema	Polydipsia. Polyuria. Severe head injury 3 years before	L. anterior cerebral compressing chiasma from above
Jefferson 1937 Case 6	F.	60	Fundi not visible. Blind both eyes	None	Recovery. Unverified

II.—Monocular Amblyopia, Central Scotoma, or Blindness (25 Cases).

Author	Sex	Age	Visual defect	Other clinical findings	Site of aneurysm
Nebel 1834	F.	28	Blind R. eye	—	Aneurysm right anterior cerebral compressing L. optic nerve
Hare 1850	F.	18	Dimness of vision L. eye	L. ptosis, 3 weeks	Died suddenly. L. posterior communicating artery compressing L. optic nerve and tract
Roe 1850	F.	21	R. eye blind 3 mths.	Violent headache 15 mths., then drowsy. Weakness L. face	Anterior cerebral aneurysm size of hen's egg, right half of sella, optic nerve and chiasma flattened. R. olfactory nerve compressed
Giraudet 1857	F.	52	Blind R. eye 2 years	Headache 2 years. Anosmia. Intelligence impaired	Aneurysm 4 × 2·5 cm. at R. side of sella, optic nerve flattened, ribbon-like
Blessig 1877	M.		L. eye blind. High-grade choke	Exophthalmos. L. 3rd nerve palsy	Internal carotid. Died 35 days after ligature
Czermak 1902	F.	59	Blind L. eye, recent	Abducens palsy, 6 years, neuralgia brow and face, 4 years. Ptosis L. recently	Aneurysm L. internal carotid found at autopsy
Beadles (Nettleship) 1907	F.	61	L. amblyopia, 18 yrs. L. optic atrophy	L. ophthalmoplegia	L. internal carotid in cavernous sinus pressing on L. optic nerve
Reinhardt 1913	M.	41	Blind L. eye	L. oculomotor palsy, complete	Not verified. X-ray destruction of sella. Recovery
Fearnsides 1916	F.	41	Blind R. eye	Anæsthesia ophthalmic division of trigeminus	Aneurysm size of small grape R. anterior cerebral
Shannon 1917	F.	52	R. central scotoma, R. optic atrophy	Paresis L. side	R. internal carotid compressing R. optic nerve
Groedel 1921	M.	41	L. optic atrophy 8 yrs. L. eye blind	L. ophthalmoplegia, slight exophthalmos	X-ray dilatation of sella. Transphenoidal operation and death from hæmorrhage. L. internal carotid, size child's fist
Cushing 1923	F.	52	Progressive amblyopia, central scotoma R.	Died suddenly some months later	R. internal carotid compressing chiasma
Cutler 1923	F.	45	Progressive failure vision R. eye. Pallor of disc. Enlarged blind spot	Nil	Died. "Circle of Willis"
Kirby 1924	M.	60	Diminished acuity, irregular contraction visual fields, pallor R. optic nerve, L. normal	Complete R. ophthalmoplegia for 34 yrs. Anæsthesia R. trigeminus. Injury 34 years ago. X-ray, mass in R. middle fossa	Necropsy. Aneurysm R. internal carotid

II.—Monocular Amblyopia, Central Scotoma, or Blindness—*Continued.*

Author	Sex	Age	Visual defect	Other clinical findings	Site of aneurysm
Packard and Zabriskie 1925	M.	21	Nasal hemianopia in R. eye only. Bilateral papilloedema	L.-sided convulsions. L. pyramidal signs	R. middle cerebral compressing R. optic nerve
Birley and Trotter 1928	M.	23	Amblyopia. Pallor R. disc	Followed severe head injury. Paresis R. 3rd, 4th and L. 6th and 7th. Violent epistaxis. Bruit present	Recovery after ligature of R. internal and external carotids
Brunetti 1931	F.	63	Failing vision, R. eye	R. ptosis	X-ray diagnosis. Calcification in region of R. internal carotid and ophthalmic arteries
Schmidt 1931	F.	53	R. amblyopia 16 years, blind 9 years	Ophthalmoplegia R., 11 years. R. trigeminal neuralgia	Aneurysm size of hen's egg, R. middle fossa compressing optic nerve
Garvey 1934	F.	55	Atrophy R. optic nerve, bilateral chorio-retinitis	Ptosis R. 2½ years. Weakness of legs. W.R. +	Aneurysm 3 cm. diameter in interpeduncular space, R. internal carotid, compressing R. optic tract, R. crus, and pons
McKinney, Acree, and Soltz 1936 (1)	M.	56	Slight pallor L. disc. R. normal. Constriction of L. visual field especially temporal	L. ptosis and ophthalmoplegia	X-ray diagnosis: calcification in aneurysm
(2)	F.	42	Pallor temporal part, L. disc. R. normal. Constriction visual field on nasal side L	Complete ophthalmoplegia L. Hypæsthesia V.1 and V.2. Bruit over eyeball	X-ray diagnosis: calcification in wall of aneurysm
(3)	M.	57	Marked pallor, L. disc. R. normal. Blind L. eye 2 yrs. R. normal	Ophthalmoplegia partial. L. hypæsthesia V.1	Unverified. Suggestive X-ray findings
(4)	F.	54	R. papilloedema. L. normal. Blind R. eye	Ophthalmoplegia R. Hypæsthesia V.1, 2 and 3	X-ray diagnosis: calcification in wall of aneurysm
De Vet and Zeckel 1937	M.	19	Became blind in L. eye, sight depressed on R. side	Complete ophthalmoplegia and anæsthesia of ophthalmic division of trigeminal, L. Wassermann + 1 in 10	Transfrontal exploration; angiographic verification. Ligature of internal carotid artery. Recovery
Jefferson—Case 5	F.	50	Pallor L. disc. Vision, R. $\frac{6}{9}$, L. $\frac{6}{6}$	L. ophthalmoplegia, incomplete. L. trigeminal anæsthesia. R. hemiparesis X-ray enlargement of superior orbital fissure. Shadow of large aneurysm in L. middle fossa	Necropsy: aneurysm size tangerine orange, L. internal carotid occupying L. middle fossa

It is difficult to see how a visual defect can be purely monocular unless the aneurysm compresses the optic nerve right up against the optic foramen, and compressed nothing else. It is certain that many cases in the Table above must have had more complex disturbances of vision than were discovered. The first three cases demonstrate this quite clearly, but both Hare's and Roe's cases must have had visual field defects in the eye which is not mentioned. A bibliographer can, however, only transcribe cases as they are recorded, however sure he may be that under modern conditions other signs would have been evoked.

III.—Monocular Amblyopia with Temporal Hemianopia in Contralateral Eye (10 Cases).

Author	Sex	Age	Visual defect	Other clinical findings	Site of aneurysm
Bramwell 1906	M.	38	Blind R. eye, temporal hemianopia on L.	Mental changes. Died 5 years later	L. internal carotid, very large
Cushing 1912	M.	31	L. homonymous hemianopia, later, blind in L. eye	None. Died suddenly 3½ years later	R. internal carotid; also a pituitary adenoma
Symonds 1924	M.	25	L. homonymous hemianopia. R. amblyopia	Infective endocarditis. Partial 3rd nerve palsy. L. hemiparesis and hemianæsthesia	Aneurysm size of hazel nut between R. optic nerve and temporal lobe
Harris 1928	F.	46	Sudden blindness, then recovery. Optic pallor, central scotoma L., temporal hemianopia R., tendency to R. homonymous defect earlier	Sudden diplopia. 7 years earlier. Recovery. None when observed	L. anterior cerebral compressing chiasma and L. optic tract
Albl 1929	M.	59	Blind L. eye, optic atrophy. R. temporal defect	X-ray, sellar distortion. Fine shell of calcification in wall of aneurysm	L. internal carotid, adherent to chiasma
Dott 1933	F.	36	L. eye blind. R. temporal defect	None	L. internal carotid
Elsberg and Dyke 1934	F.	57	1933—Amblyopia L. eye. 1934—L. eye blind. R. temporal hemianopia	None	Operative verification; aneurysm 2 × 2 cm., origin not discerned. Recovery
McKendree (1) and Doshay 1936	F.	46	Pallor R. disc, L. normal. Almost blind R. eye, temporal field defect L.	Nil. X-ray negative	Operative disclosure of intrasellar aneurysm
(2)	F.	31	Blind L. eye, fundi normal. Temporal defect R. field	Amenorrhœa 10 yrs. Sella porosed, not enlarged	Operative disclosure of intrasellar aneurysm
Jefferson—Case 8	F.	49	Atrophy R. disc, blind. Pallor, L. temporal hemianopia	Sella normal. Shell of suprasellar calcification on X-ray	Thorotrast verification

[1] In the above group the temporal defect was, no doubt, sometimes due to a tract compression and was basically part of a homonymous hemianopia. In other cases it was due to compression of the chiasma and would be part of a bitemporal visual loss. My own Case 8 was of the latter kind.

IV.—Homonymous Hemianopia (11 Cases).

Author	Sex	Age	Visual defect	Other clinical findings	Site of aneurysm
Henneberg 1906	F.	40	L. homonymous hemianopia. Flickering lights before L. eye	Headache. Pain, R. trigeminal area, 14 days, then several epileptic fits. Died in stupor	Aneurysm L. anterior cerebral 1 cm. long in olfactory trigone, compressing L. optic nerve.
Gehrung 1914			Homonymous hemianopia	——	Internal carotid.
Freund 1916	F.	70	R. hemianopia, 8 years. Normal eye-grounds.	Tabes dorsalis. W.R. +	L. internal carotid, spindle-shaped aneurysm pressing on L. optic tract.
Foerster 1921	M.	20	Sudden blindness both eyes, vision returned. Later hemianopia	L. hemiplegia	Middle cerebral.
Aliquo-Mazzei 1929	M.	61	R. homonymous hemianopia. Pallor of both discs	Complete R. Ophthalmoplegia	R. internal carotid.
Dott 1933	M.	58	R. upper quadrant incongruous homonymous hemianopia	None	R. anterior cerebral.
Sjoqvist, O. 1936	M.	72	Retinitis. No optic atrophy. L. homonymous hemianopia	Anosmia. Psychological changes. Arteriosclerosis	Large R. carotid aneurysm demonstrated by thorotrast.
Jefferson—					
Case 1	M.	47	L. homonymous hemianopia. Fundi normal.	History of subarachnoid hæmorrhage. Slight L. hemiparesis. Later fits	Unverified pathologically. Recovery.
Case 2	M.	38	R. homonymous hemianopia. Fundi normal	History of subarachnoid hæmorrhage. Dysphasia. Later fits	Recovery. Unverified pathologically.
Case 3	F.	54	Fundi normal. Acuity normal. R. homonymous hemianopia	Visual epilepsy in R. visual field	Recovery. Unverified.
Case 4	F.	29	Amaurosis, recovery; then L. homonymous hemianopia. Fundi normal	History of subarachnoid hæmorrhage. R. 3rd nerve palsy. R. trigeminal hypæsthesia. L. hemiparesis	Necropsy: aneurysm R. posterior cerebral compressing optic tract and crus.

V.—Bitemporal Hemianopia (15 Cases).

Author	Sex	Age	Visual defect	Other clinical findings	Site of aneurysm
Weir Mitchell 1889	M.	43	Bitemporal hemianopia 2 yrs. Pallor of discs	Attacks of weakness in arms and legs, occasional dragging R. foot. Sudden coma and death	Aneurysm dorsal to chiasma (? abnormal anterior arteria communicans), separating optic nerves
Noiszewski 1901	M.	31	Bitemporal hemianopia, choked discs	None	L. carotid artery tied. Recovery
Bramwell 1906	M.	31	Bitemporal hemianopia, later completely blind	Dementia later. Injury 15 years before	R. internal carotid, size of orange, stretching optic nerves
Kümmell 1911	M.	37	Bitemporal hemianopia, then R. eye blind. L. vision in lower visual quadrant only	None	R. internal carotid (? R. anterior cerebral)
Posey 1911	F.	62	Bitemporal hemianopia, bilateral optic atrophy	None	L. internal carotid pressing on chiasma
Conway 1926	M.	23	Bitemporal hemianopia, then blindness in both eyes, later return of vision	None. Died suddenly after 9 mths.	R. middle cerebral
Foggie 1927	F.	56	Bitemporal hemianopia. Trace of papilloedema R. L. normal	R. ophthalmoplegia 4 months. Headache, vomiting, 5 weeks. Severe pain and anæsthesia R. forehead	Recovery. Condition not much changed one year later
Pfingst and Spurling 1929	F.	54	Bitemporal hemianopia	Sudden recurrent 3rd nerve palsies	X-ray : calcified area lying to R. of sella. Recovery
Trevani 1934	M.	34	Progressive bitemporal hemianopia 3 years ; blind L. eye 1 year. Primary optic atrophy	None	Operation. Aneurysm $5 \times 4 \times 3$ cm. internal carotid L.
Sjoqvist, O. 1936	M.	58	1924 temporal hemianopia R. eye. Later blind both eyes	Hypopituitarism. Sellar destruction 1934	Died after operation. Huge aneurysm filling sella turcica
Wakeley 1937	M.	44	Bilateral optic atrophy. Bitemporal hemianopia. 10 years' history	Epileptic fits recently. X-ray, suprasellar calcification	Operative and post-mortem verification. Aneurysm of anterior communicating artery
Jefferson— Case 7	F.	36	Pallor R. disc, acuity $\frac{6}{9}$. L. normal, $\frac{6}{\frac{6}{12}}$. Bitemporal hemianopia	None. Sella normal	Operative verification. Aneurysm of R. anterior cerebral artery
Case 10	F.	56	V.A.R. $\frac{6}{4}$, V.A.L. C.F. L. disc pale. L. central scotoma, bitemporal defects	None except enlargement of sella	Operative verification, aneurysm L. internal carotid (infra-clinoid)
Case 11	M.	23	Pallor of both discs. V.A.R. $\frac{6}{18}$, L. $\frac{1}{60}$. Bitemporal hemianopia	Enlarged sella, erosion L. optic canal	Operative verification. L. internal carotid ligatured. Recovery
Case 12	F.	46	R. optic atrophy, acuity $\frac{6}{60}$. L. disc normal, acuity $\frac{6}{5}$	R. abducens paresis. L. paresis superior rectus. X-ray : enlarged sella. Amenorrhœa 8 years	Operative verification. R. internal carotid

VI.—Varia (9 Cases).

Author	Sex	Age	Visual defect	Other clinical findings	Site of aneurysm
Rice 1904	F.	65	Failing vision for 10 years	Epilepsy	R. anterior cerebral size 3·4 × 2·9 cm. pressing on chiasma and R. optic nerve
Kennedy 1916	F.	53	Blind R. eye, pallor of disc. Central scotoma, L. eye	Slight weakness L. arm, depressed abdominals, L.	Died. R. internal carotid
Taylor 1923	F.	46	V.A.R. and L. $\frac{6}{60}$. Six months later L. eye blind, limited central vision on R.	Nervous breakdown and diplopia some years before	Died. Large sac from anterior cerebral artery compressing both optic nerves
Denray *et al.* 1926	F.	32	Failing vision	"Meningismus" 3 years earlier. Second attack followed by insanity	R. internal carotid, compressing the chiasma
Lodge, Walker and Stewart 1927	F.	52	Amblyopia L. eye, 9 months. R. 2 months. Later, blind L. eye, nasal field defect R. eye	Polyuria. Finally sudden flashes of light before eyes. Vomiting, coma. Died suddenly	L. internal carotid; 3·5 cm. diameter, deeply projecting into interpeduncular space. Optic tracts and chiasma stretched ribbon-like over the mass
Schmidt 1931	F.	40	Amblyopia R. eye, later blind. Later, failing vision L. eye	None	Spherical aneurysm, size of plum. R. internal carotid compression chiasma
Cutler and Zabriskie 1933	M.	25	Blind R. eye. Primary atrophy. Failing vision L.	Palsy R. 6th and partial of 3rd nerve. Anæsthesia R. $V^1 + V^2$. (Injury 8 years before). Large sella	Huge aneurysm R. internal carotid, chiasma elevated and pushed to L. Aneurysm filled anterior part of R. middle fossa. Post-mortem
Sjoqvist, O. 1936	M.	48	Inferior quadrantic binasal hemianopia. Later L. eye blind from retinal thrombosis	Blood-pressure 300 Hg. Anosmia	Presumptive diagnosis after thorotrast injection. L. internal carotid aneurysm
Jefferson—Case 9	M.	59	Bilateral optic atrophy. V.A.R. $\frac{1}{60}$. V.A.L. $\frac{6}{24}$. Altitudinal hemianopia	X-ray: calcification of sellar aneurysm	Thorotrast verification. L. internal carotid

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OBSERVATIONS ON DYSTROPHIA MYOTONICA.

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SUMMARY.

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OBSERVATIONS.

The present report includes the results of examinations of 57 families in which one or several members suffered from dystrophia myotonica.

	Male	Female	Total
Severe cases	61	26	87
Milder cases	15	25	40
Suspicious cases	69	76	145
Slightly suspicious cases ..	26	34	60
	171	161	332

In addition twenty male members and nine female members of these families whom it was not possible to examine were said to be affected with dystrophia myotonica. It is probable that these cases were severely affected, as mild symptoms would have remained unobserved.

The above figures show that severe degrees of dystrophia myotonica were more frequently observed in members of the male sex, but the higher number of females who were slightly affected, or presented suspicious signs, make it probable that females are affected with the taint of this disease as often as males, although the signs do not develop in the same degree.

A sharp differentiation between severe and milder cases cannot be made. I have called those cases " severe " in which myotonia, wasting and weakness were marked, but even some of those affected in pronounced degree did not feel much disability and were still at work. It was doubtful whether other cases should be called " mildly affected " or " suspicious " cases.

Five families were Jewish, the other families were British or German.

Myotonia.—The characteristic myotonia after active movements could not be observed in every case, not even in every severely affected case, although it became conspicuous on mechanical excitation. This difference between active movements and mechanical excitation was observed in six cases.

In several other severe cases myotonia on active movements was present in slight degree only, but was very marked on mechanical excitation. In many mild cases myotonia was very conspicuous on mechanical excitation, but was not observed on active movements. But although myotonia on active movements was not found in these persons, it probably was not completely absent, as several of them reported that they felt stiffness in their hands at certain times. In one mild case myotonia was present on active movements, but was very feeble on mechanical excitation.

These results demonstrate that the examination by mechanical excitation is often a more valuable test than examination by active movements.

A striking variability in myotonia was observed in one patient; as he was an in-patient in a hospital there was the opportunity of examining him repeatedly. Myotonia was very conspicuous on certain days, but was completely absent on other days. As far as could be determined this variability did not depend on the temperature of the air. It is well known that myotonia comes on in cold much more than in warm weather. Another patient reported that stiffness in his limbs disappeared after movement, a fact mentioned by many patients and frequently observed on examination. He stated further that stiffness was much worse on the day following unusually prolonged exercise—for example, on the day after he had played tennis for more than one hour. In one severe case a remarkable disturbance on active movements was observed; when he brought his arms up, or when he bent his forearms or straightened his fingers, these movements were done in the well-known slow way, but at certain intervals clonic jerks interrupted the

slow movements for a few seconds. When the intended movement was performed his fingers and the flexor surface of his hands sweated profusely. A brother of this patient also suffered from dystrophia myotonica, but this unusual disturbance was not seen in his case.

The myotonic reaction on mechanical excitation was usually most conspicuous in the tongue and in the small muscles of the hand, but was not confined to these muscles. In many patients who could be examined in bed myotonia was observed in nearly all striated muscles, probably more often in the extensors of the forearm than in the flexors.

Muscular wasting.—Some authors have found that certain muscles are especially affected in dystrophia myotonica, viz. the facial muscles, sternomastoids, brachio-radialis and small muscles of the hands, while other muscles, especially those of the shoulder-girdle and of the pelvic-girdle, remain more or less unaffected. But no definite rule can be formulated as to which are most affected. No wasting of the facial muscles was found in two definite cases. The sternomastoids were unaffected in five cases, all of which occurred in the same family, and the brachio-radialis was not wasted in several severe cases.

A general wasting of the forearms was observed in a case in which the brachio-radialis was not more affected than other muscles. Neither the hand muscles, forearms nor arms were wasted in one severe case, but the sternomastoids as well as the facial muscles were atrophied and the lower limbs were weak: she walked with typical stepping gait and myotonia as well as cataract was well developed. No wasting of his limbs was observed in one case when aged 27 years, but seven months later slight wasting of his left hypothenar, and doubtful wasting of his left thenar, eminence were observed.

One man presented definite affection of the muscles of his shoulder and pelvic girdles. His scapulæ were winged and he had great difficulty in getting up from a lying position without using his hands, like a case of myopathy. Slight atrophy only was observed in his sternomastoids, brachio-radialis, and the small muscles of his left hand and in all muscles of his lower limbs. This case has already been mentioned in connection with the variability of the mechanical myotonic reaction in his limbs.

A conspicuous weakness in the pelvic-girdle was found in a patient (Mrs. C. J., 1 (ii) 6)[1] who had much difficulty in getting up from a

[1] Where family trees are published the position in the family of the patient referred to is indicated in this manner.

sitting position but in whom other signs of dystrophia myotonica were not marked.

In another case some muscles of the shoulder-girdle were weak and the scapulæ were winged, although neither wasting nor weakness were very marked in his upper limbs; myotonia was especially conspicuous in his tongue and in his hands.

These cases demonstrate that no definite rule can be given as to which muscles waste early, although certainly in the majority of cases the temporals, cheeks, sternomastoids and small muscles of the hands are more or less wasted and weak.

In greatly wasted muscles the myotonic reaction was usually absent. In one case in which all the muscles of the limbs were greatly wasted and paralysed, in only a small part of the left thenar group could a myotonic reaction be produced by mechanical excitation; this patient reported, however, that she had felt the characteristic stiffness on active movements when her disease began many years ago.

No person suffering from definite myotonia but perfectly free from wasting was examined. The diagnosis of "Thomsen's Disease" was therefore not made, but in four patients who were affected with myotonia, wasting could be observed in a few muscles only.

In one man, aged 34, a case of myotonia dating from infancy, hypertrophy was observed in the upper and lower limbs, especially in the deltoids, trapezii, biceps and quadriceps on both sides, while there was slight wasting in the facial muscles and sternomastoids and probably also in the peronei. Strength was everywhere poor, though he stated that in his boyhood he had been exceptionally strong. His brother was similarly affected; he suffered from stiffness in his limbs and sometimes cramp in his neck muscles, but on examination myotonia and wasting were only slight though there was marked weakness of many muscles.

Asymmetry of the muscular wasting was observed occasionally. In Albert B., who was observed at the age of 20, the cheeks were definitely thin, the left brachio-radialis was smaller than the right, the left thenar muscles were flatter than the right, and the temporals were suspicious of early wasting. In Arthur B. (aged 26), in whom myotonia was present from infancy, the temporals were slightly wasted, the cheeks were a little thin, the left sternomastoid was definitely wasted by comparison with the right, and the lateral parts of both thenar eminences were also slightly atrophied. In another case dating from infancy, the temporal muscles had been wasted for about fifteen years. His cheeks were thin,

but were not definitely pathological. His left thenar eminence was flatter than his right, the proximal end of his left supinator appeared to be thinner than his right, and all muscles in the upper and lower limbs were small. His obliqui abdominis also appeared to be wasted.

Tendon reflexes were often absent in mild cases as well as in severe. They were preserved, however, or only one or more absent, in some severe cases. For example, in a man aged 56, who was very severely affected, the left supinator reflex only was absent, and in another severe case the right knee-jerk and both ankle-jerks were present.

Cataract.—It is noteworthy that cataract, a sign observed so often in cases of dystrophia myotonica, was absent in the four patients in whom signs of muscular wasting were observed in an unusually slight degree, whilst myotonia was marked. In another patient (12 (iii) 4) who was free from cataract, myotonia as well as intellectual defects were marked, whereas wasting of muscles was slight. The muscles in his thighs, as well as his deltoids, were especially well developed and were perhaps pseudo-hypertrophic, as their strength seemed to be rather poor compared with their volume.

One mild case (9 (c) (iii) (2) 4) is of interest in this connection. Signs of dystrophia myotonica were observed in her mother, her brother and her two sisters. Myotonia was conspicuous in her tongue and her hands, and there was slight atrophy in her right thumb and definite weakness on closing her eyes and blowing out her cheeks. No cataract was found at the time of the first examination, but fifteen months later Mr. Goulden observed a few suspicious green crystals in the anterior part of her lenses. Her mother had been operated on for cataract at the age of 44, and in her brother and in two sisters evidence of cataract had been observed on slit-lamp examination.

Cataract presenting the peculiarities which are generally regarded as characteristic of dystrophia myotonica [13] was observed in several brothers and sisters of patients suffering from this disease, in whom only suggestive evidence of muscular disturbances could be found. As all healthy siblings were not submitted to a slit-lamp examination, it is impossible to give the proportion in which cataract was the only definite sign.

In two "healthy" mothers of patients cataract was observed on slit-lamp examination. In one no other suspicious sign was observed, but in the other, besides cataract which produced no trouble, there was a suspicious myotonic reaction to mechanical excitation of the thenar muscles, slight wasting of the facial muscles and on electrical examina-

tion "the thumb muscles of both hands required a strong faradic current to elicit a contraction. There was a tendency to a slow, sluggish response to the interrupted galvanic current and a suggestion of hypertonicity to the constant galvanic current."

It is of interest that in several cases alterations in the lenses were observed which were suspicious of the typical cataract, but which were so slight that the ophthalmic surgeon conld not give a definite opinion. One case of this kind was mentioned on page 502 (9 (c) (iii) (2) 4). Two other cases had only suspicious muscular abnormalities.

(1) Eileen D., aged 18, the cousin of a severe case, had been mentally deficient since infancy. There was no myotonia, but definite wasting of the right sternomastoid and doubtful atrophy of the left brachio-radialis and left thenar muscles. Examination by slit-lamp gave "a few fine sparkling angular opacities, throughout the lens cortex in each eye, very few glistening coloured spots, suspicious of the commencement of cataract."

(2) Arthur G. R. (1 (iii) (4) 5), aged 21, whose father, brothers and sisters suffer from dystrophia myotonica was mentally very defective. There was a suspicious myotonic reaction to mechanical excitation of the tongue and thenar muscles, with slight wasting of the temporals, doubtful wasting of the right peroneal muscles, and weakness on blowing out the cheeks and in dorsal flexion of the feet. Examination by slit-lamp gave "Fine odd opacities in both nuclei, a congenital condition commonly found. A few angular opacities in the cortex of both lenses, which are probably due to myotonia, but require confirmation at a later date."

These cases indicate that some siblings may show suspicious signs of cataract as well as of the muscular affection, but a definite diagnosis of dystrophia myotonica could not be made.

Testicular atrophy.—Like other authors I observed small and soft testes in many severe and mild cases, and many of my patients also reported disturbance of sexual power. Two patients, however, became fathers in advanced stages of dystrophia myotonica. F. (1 (ii) 4) at the age of 36 was an in-patient at the National Hospital, where he was found to be severely affected with this disease. His seventh and his eighth children were born when he was aged 37 and 39. John (1 (ii) 5), his step-brother, was an in-patient at the National Hospital at the age of 31. His testes were soft, but he became a father in the same year and again eleven years later. So-called secondary sexual characters were poorly developed in the majority of definite cases.

Baldness was often present, more frequently in male patients than in female; it started usually at the sides of the forehead, but its diagnostic value as a sign of dystrophia myotonica is not important.

Enlargement of the thyroid does not seem to be very uncommon. It was present in six more or less severe female cases and in two severe male cases. One severe female case is reported to have had a goitre at the time when she began to suffer from dystrophia myotonica. Thyroid enlargement was also seen in several suspicious cases.

Classification of Cases.

I have called "suspicious" and "slightly suspicious" cases all relatives of definite cases in whom only one or other sign of dystrophia myotonica was observed.

In many of these cases typical myotonic contraction of muscles was found on mechanical excitation, especially in the tongue and thenar or hypothenar muscles.

It is well known that the degree of reaction to mechanical excitation is not the same in every normal person. In some the thenar muscles contract after mechanical excitation up to complete opposition of the thumb, but the contraction comes on quickly, not slowly as in a typical case of dystrophia myotonica, and relaxation, also, is less delayed than in this disease.

In a certain number of persons in affected families the contraction of the thenar and hypothenar muscles after mechanical excitation occurred at a rate more or less mid-way, so that it was impossible to decide whether the contraction was normal or pathological.

In the majority of "suspicious cases" there was more or less marked wasting of muscles, particularly in the facial, sternomastoids and thenar muscles and weakness of the dorsiflexors of the ankles; in some cases also there was general wasting in the neck and upper and lower limbs.

It is well known that the temporal muscles and cheeks are wasted in many healthy persons in old age, as well as in young persons who suffer from a wasting disease, such as cancer or tuberculosis of the lungs, but only as an exception have I observed wasted facial muscles in healthy young persons.

The following two patients, cousins of typical cases but not themselves suffering from dystrophia myotonica, showed a myotonic reaction to mechanical excitation:—

(1) Clara S. (9 (b) (ii) 2), aged 53, had slight wasting of the temporals and a definite myotonic reaction in her tongue and a suspicion of it in the thenar muscles. She had a poor grip and the right triceps reflex was absent.

(2) Mary F. (9 (b) (ii) 6), her sister, aged 42, suffered from "neuritis" in her upper limbs eight years ago. On examination there was slight wasting in

her temporals, a definite myotonic reaction in her tongue, and her thenar muscles gave a response suspicious of the myotonic reaction on mechanical excitation. Her grip was poor.

Wasting of a sternomastoid in persons not suffering from dystrophia myotonica is demonstrated by two cases :—

(1) Herbert Geo. (9 (a) (ii) 3), the cousin of typical cases of dystrophia myotonica, aged 44, feels healthy and is at work. The right sternomastoid was definitely wasted (fig. 1), the left brachio-radialis not so well developed as

FIG. 1.

the right, which was also not quite normal. Probably there was some weakness on shutting the eyes and a certain degree of hypertrophy of the flexors in both forearms. These observations were confirmed by Dr. Riddoch.

(2) Mrs. D., aged 76, had one son and several grandchildren suffering from dystrophia myotonica. She felt and looked perfectly healthy. The left sternomastoid was, however, wasted and the left thenar muscles slightly so. Occasionally there was myotonic reaction to mechanical excitation in the left hypothenar muscles. The supinator and triceps reflexes were absent. On slit-lamp examination no cataract was observed.

Wasting of the facial muscles is illustrated by the following cases :—

(1) Alfred T. (9 (c) (ii) 3), aged 45, whose brother and sister suffer from dystrophia myotonica, had complained of cramps in his hands and lower limbs

for fifteen years. His haggard face was typical of dystrophia myotonica; his cheeks are thin and the temporals wasted. There is probably weakness on blowing out his cheeks and the left thenar muscles are flatter than normal; there is doubtful myotonic reaction to mechanical excitation in the left trapezius and the right triceps. The muscles in the lower limbs are fairly thin. There is a typical early cataract.

(2) Frederick J. D. (10 (iv) 3) was aged 22. A paternal uncle as well as a sister suffer from dystrophia myotonica. He feels perfectly healthy. On examination definite wasting of the temporals was found and his face was thin. There is a suspicion of myotonic reaction to mechanical excitation in the extensors of both forearms and a weakness of dorsal flexion of both feet. Otherwise he is normal in every way and has no cataract.

As an example of wasting of the small muscles of the hand, especially often observed in suspicious cases, I may mention Mrs. G. (2 (ii) 10), aged 87, many of whose nephews and nieces suffer from dystrophia myotonica (*vide* Greenfield [14]). Her memory is disturbed, probably as a result of old age, but her behaviour is normal. She has suffered from cataract for many years. There is definite wasting in both thenar muscles, but no myotonic reaction. Several similar cases were observed.

Weakness of muscles was often seen in "suspicious cases," especially of those affected in definite cases of dystrophia myotonica, for example, in the facial muscles, the flexors of the fingers and the dorsiflexors of the feet. One of the "suspicious cases," the brother of three sisters suffering from dystrophia myotonica (Family Hur.), was free from definite signs of the disease, but he could not blow out his cheeks properly. It is noteworthy that in some mildly affected, as well as in some "suspicious," cases the lateral part of the thenar group only was wasted, whilst the inner part seemed to be normal. One case of this kind is the following:—

Thomas B., aged 24, whose brother had suffered from myotonic disturbance since infancy but in whom only a few muscles were wasted, felt healthy but he reported that he could not play a trumpet as long as other members of his orchestra because the muscles of his mouth tired quickly, and his hands also tired rapidly when playing the piano. On examination there was slight wasting of the left abductor pollicis and a suspicion of general wasting of the forearms. The left sternomastoid was probably not so well developed as the right and the grip was not strong. There was a definite myotonic reaction to mechanical excitation in the hypothenar muscles.

A similar condition was found in other cases.

Electrical Reaction of Muscles.

The reaction to faradic and galvanic currents gave valuable results in "suspicious" and "slightly suspicious" cases. Dr. Bailey was kind enough to make these examinations.

The electrical myotonic reaction described by Erb [9] is generally regarded as characteristic of myotonia congenita (Thomsen's disease) and dystrophia myotonica. It has also been observed in a few cases of another nature by Hoffmann and by Kramer [16] and by Falta [11]. Dr. Martin observed such a case in the National Hospital (S.Mc.L.), probably as a result of thyroid deficiency; she had a rough dry skin and myotonic reactions on electrical excitation, mechanical excitation and active movements, which completely disappeared after treatment with thyroid extract. Such cases can be disregarded, as the characteristic signs of endocrine deficiency are present.

Four cases in which by other methods of testing only a few suspicious signs of dystrophia myotonica were found, but in which there was a definite myotonic reaction on electrical examination, may be mentioned.

(1) Catherine May D., aged 26, is a nurse and feels healthy. A brother and sister of her father suffered from dystrophia myotonica. On examination there was found slight myotonic reaction in her tongue and slight wasting in the lateral part of both thenar muscles. The temporals were slightly wasted and the grip was poor. No cataract was found on slit-lamp examination. On electrical examination "the right and left opponens pollicis were stimulated by means of the interrupted faradic and galvanic currents. Faradic response was obtained with an extremely small current incapable of stimulating a normal muscle. Galvanic response was obtained with 2 ma. of current, whereas in a normal muscle 5-6 ma. were necessary. The galvanic response was also obtained at the make and break of the current with 4 ma. The continuous uninterrupted current tetanized both muscles with 5 ma. The above findings show definite hyper-excitability to both the faradic and galvanic currents. i.e. *a myotonic reaction.*"

(2) Ernest G. L., aged 26, a student whose maternal uncle suffered from dystrophia myotonica, feels healthy. The left thenar and both hypothenar muscles gave suspicious myotonic reactions to mechanical excitation. There was slight wasting of the left abductor pollicis and the temporals were slightly atrophied. There was a possible weakness in blowing out the cheeks. On electrical examination, "the thenar and hypothenar muscles of both sides responded to a weak faradic current, insufficient to produce contraction in a normal muscle. The muscles also contracted well to an interrupted galvanic current of 6 ma. A contraction was obtained to make and break of current at 10 ma. in the right opponens pollicis. There was a tendency for the

constant current to tetanize the muscle. The evidence is in favour of hyperexcitability of muscle-fibres, *therefore of an early myotonic reaction.* There was slight wasting of the abductor pollicis of the left side, but its electrical reaction still showed some hyperexcitability."

(3) In John Edward M., aged 14, whose brother, aged 32, suffers from dystrophia myotonica and whose mother, another brother and a sister are affected with typical cataract, there is a doubtful wasting in the temporals; otherwise he was normal. There is no cataract. On electrical examination, "the left thumb is normal. In the right thumb the faradic response is normal, but with an interrupted galvanic current the response of the abductor and opponens pollicis is sluggish in character, the relaxation being slow, possibly due to tetany. With 6 ma. of current a contraction in both these muscles was elicited at the make and break of the current. This was not the case in the left thumb. No one of these muscles was wholly tetanized with the constant current."

(4) Charles D. (6 (iii) (1) 3), aged 34, whose mother, brother and sister suffer from dystrophia myotonica, showed a myotonic reaction in the tongue, slight wasting in the temporals and both tibialis anticus muscles, and dropping of both upper lids. There was weakness in the peroneal muscles; the closing of the eyes was also probably weak; the supinator and triceps reflexes were absent. On electrical examination slight tetanic contraction of the left side of the tongue was observed with $2\frac{1}{2}$ ma. current.

In many other cases, both of definite and suspicious character, the electrical reactions were abnormal. Though in several suspicious cases no abnormality was found, electrical testing must be regarded as a valuable method of investigation in all doubtful cases.

In this connection a case reported by Babonneix [2] is remarkable. He observed a myotonic electrical reaction in a man who was absolutely free from other signs of myotonia, but who was a brother of a patient with Thomsen's disease.

It would have been valuable if the results of electrical, and still more of mechanical, stimulation could have been recorded in a graphic manner, but unfortunately this was impossible at the time of examination.

Age of Onset of Dystrophia Myotonica.

It has been often stated that dystrophia myotonica starts after the age of 20 or 30, whilst Thomsen's disease is an inborn affection. My own observations demonstrate, however, that dystrophia myotonica often begins in early infancy.

John Kenneth R. (1 (iii), (5) 4) a boy of $3\frac{1}{2}$ years, the son of a severe case of dystrophia myotonica, gave definite myotonic reactions to mechanical excitation in the thenar and hypothenar muscles.

Anita R., aged $6\frac{3}{4}$ years, the sister of a severe case, showed a definite myotonic reaction of the tongue and probably also of the right thenar muscles, and weakness of the facial muscles.

In the following patients, most of whom suffered severely from dystrophia myotonica, symptoms of the disease had been noticed in early life :—

Otto B. (8 (ii) 3), aged 34, felt stiffness in his hands at 8.

Bernard B. (8 (iii) (2) 1), aged 18, noticed stiffness in his hands at 12 ; his mother, who had observed the development of the disease in his father, reported that her son's voice became raucous like his father's when he was only 7 years of age.

Leslie W. (7 (iii) 5), aged 13, had, when examined at the age of 9, facial weakness, defective speech, stepping gait and enlarged muscles.

In seventeen other patients who were examined symptoms of the disease had been noticed during childhood or adolescence.

I have observed also in numerous relatives of patients definite signs of the affection, such as myotonia on mechanical excitation, and in some of them also on active movements, slight wasting or weakness of muscles, absence of one or other of the tendon reflexes, or typical early cataract which produced no disturbance of eyesight, in persons unaware of any symptoms of the disease. In such cases it is uncertain when these abnormalities first appeared.

I examined also many children of patients suffering from dystrophia myotonica in whom one sign or other of the disease was present, but whether, and at what time of life, they will suffer from any disability is at present unknown. Several patients affected with definite signs of dystrophia myotonica had been mentally defective since infancy. As they had not been specially examined in infancy we do not know when these signs first appeared.

These patients who had symptoms characteristic of dystrophia myotonica in childhood, as well as the children in whom I observed these signs, prove that dystrophia myotonica certainly often starts at quite an early age.

Observations on Sibships in which One Member at least was a Definite Case of Dystrophia Myotonica.

(1) *Number of Affected, Suspicious and Healthy Persons in these Sibships.*

I observed one or more definite cases of dystrophia myotonica in 69 sibships in 55 families. Two families which were examined later

have not been considered in the following statistics. Eighty-four miscarriages and deaths in infancy were reported in these 69 sibships and 59 persons had died in later life. Nothing was known of 54 members who had grown up. In all, 215 persons were examined in these 69 sibships.

The results are summarized below :—

	Male	Female
Severely affected	53	35
Mildly affected	19	22
Suspicious cases	32	29
Slightly suspicious cases	8	6
Healthy cases	7	4
	119	96

An exact statistical examination of the disease in the affected sibships is not possible at present, as many members were not examined, and among those examined 75, or 35 per cent., presented only suspicious or slightly suspicious signs and 11 no suspicious signs at all. A considerable advance in this direction, however, could be made if more objective and exact methods of examination could be applied to suspicious and "healthy" cases.

(2) *The relation of birth order to severity of signs.*

In order to discover whether the incidence or severity of the disease had any relation to a patient's position in the family, I asked Dr. L. S. Penrose to analyse the results of my examinations up to June, 1936. He has compiled Table I and has given the following report :—

"We find that the severe cases are less frequently found at the beginning of the family than is to be expected. This conclusion applies also to the milder cases. Similarly, there are more severe and milder cases than are to be expected if we take the birth rank from the fifth to the twentieth. This effect is not very marked and it is possible that it may be accounted for by the fact that those severe cases which occur early in the family died before one had an opportunity to examine them. Thus the group of 'died' and 'miscarriages' shows a marked excess of the first-born above the expectation (22 against 14·87). The figures certainly suggest that severe cases tend to occur towards the end of a family, but no definite conclusion can be arrived at. There may be a main gene responsible for dystrophia myotonica and numerous modifying influences, one of which may be associated with birth order."

TABLE I.

Birth rank	N		U_1		U_2		S_1		S_2		A_1		A_2		Total	
	T.	Exp.	T.	Exp.	T.	Exp.	T.	Exp.	T.	Exp.	T.	Exp.	T.	Exp.	T.	Exp.
1	2	1·14	5	4·86	22	14·87	1	1·44	5	8·58	7	8·09	8	11·02	50	50·00
2	—	1·14	7	4·86	14	14·87	2	1·44	9	8·58	9	8·09	9	11·02	50	50·00
3	—	0·14	3	5·20	15	13·37	2	0·94	11	7·24	7	7·59	4	7·54	42	42·02
4	—	0·14	5	4·53	13	12·04	—	0·94	5	5·91	6	6·59	7	5·86	36	36·01
5	—	0·14	2	4·28	13	10·97	—	0·94	7	5·45	7	6·37	4	4·86	33	33·01
6	—	0·14	4	3·75	6	9·54	2	0·94	2	3·89	5	4·09	7	3·66	26	26·01
7	—	0·14	3	2·86	7	7·22	1	0·60	1	2·05	2	2·97	4	2·10	18	17·94
8	—	0·14	2	2·13	8	5·49	—	0·57	—	2·05	3	2·94	2	1·67	15	14·99
9	—	0·14	2	1·44	3	3·67	—	0·35	1	0·84	1	0·71	1	0·84	8	7·99
10	—	0·14	—	1·33	2	2·67	—	0·35	1	0·84	1	0·27	2	0·39	6	5·99
11	1	0·14	1	1·23	1	2·47	—	0·05	2	0·74	—	0·07	—	0·29	5	4·99
12	—	0·05	1	0·68	1	1·74	—	0·05	1	0·29	—	0·07	—	0·11	3	2·99
13	—	0·05	1	0·68	2	1·74	—	0·05	—	0·29	—	0·07	—	0·11	3	2·99
14	—	0·05	1	0·68	1	1·74	—	0·05	—	0·29	—	0·07	1	0·11	3	2·99
15	—	0·05	2	0·11	—	1·39	—	0·05	—	0·29	—	0·00	—	0·11	2	2·00
16	—	0·05	—	0·11	—	1·39	1	0·05	1	0·29	—	0·00	—	0·11	2	2·00
17	—	0·05	—	0·05	—	0·70	—	0·05	1	0·10	—	0·00	—	0·05	1	1·00
18	1	0·05	—	0·05	—	0·70	—	0·05	—	0·10	—	0·00	—	0·05	1	1·00
19	—	0·05	—	0·05	—	0·70	—	0·05	1	0·10	—	0·00	—	0·05	1	1·00
20	—	0·05	—	0·05	—	0·70	—	0·05	—	0·10	—	0·00	1	0·05	1	1·00
Total	4	3·99	39	38·93	108	107·98	9	9·01	48	48·02	48	47·99	50	50·00	306	305·92

N = normal.
U_1 = not examined.
U_2 = died (this includes miscarriages)
S_1 = suspicious.
S_2 = slightly suspicious.
A_1 = mild affection.
A_2 = severe affection.

The most affected member of the sibship was :—

The youngest in twenty-six sibships of the following number of siblings : 9, 10, 6, 6, 5, 6, 6, 9, 20 (?), 6, 5, 7, 4, 2, 3, 2, 3, 2, 3, 2, 2, unknown, 6, 4, 3 (?), 5, 3, 3.

The 10th in one sibship of 11.
,, 8th ,, ,, ,, ,, 11.
,, 7th ,, ,, ,, ,, 8.
,, 5th ,, ,, ,, ,, 11.
,, 4th ,, three sibships ,, 6, 8, 8.
,, 3rd ,, two ,, ,, 4 and 7.
,, 2nd ,, ,, ,, ,, 3 and 5.
,, 1st ,, eight ,, ,, 2, 2, 4, 4, 5, 6, 7, 8.

In six sibships several members were equally affected with severe signs.

The figures submitted to Dr. L. S. Penrose cannot be regarded as final, as in several of the sibships the younger members were still young, so that we have no present knowledge which member will eventually be the most affected. In this connection a sibship may be mentioned (2 (iii) (8)) which was described by Greenfield in 1911 [14]. The

youngest, aged 25, had no symptoms of dystrophia myotonica in 1910, but he was as seriously affected as the 10th, the 12th, and the 13th members of the sibship when I examined them in 1935.

In three other sibships, in whom the patient was the eldest, the youngest were respectively only 7, 11 and 14 years of age.

Probably the effect of birth order may be counterbalanced in some sibships by the influence of sex. As stated in the beginning of this paper, severe cases were observed more frequently in males than in females. The influence of sex may thus explain why in several sibships the youngest *male* member was most affected, while younger female members were less affected. As examples of this supposed influence of sex, the following sibships may be mentioned :—

(1) A patient, male, was the 10th of 11 ; the 11th, a female, was a definite but less severe case.

(2) A patient, male, was the 4th of 8 ; the 5th and the 6th, both male, had died ; the 7th and the 8th, both female, were less seriously affected than the 4th.

(3) Karl S. (12 (ii) 4), male, was the 4th of 9 ; the 5th, female, was less affected ; the 9th, female, was unaffected ; the 6th, 7th and 8th had died in youth or in infancy.

The influence of birth order is best seen in sibships of which numerous members could be examined and in which only the youngest was severely affected, e.g. Family T. (9).

Certainly an influence of birth order is not evident in all the sibships examined by other authors, but in several large sibships which have been recorded only the youngest members were severely affected. (Curschmann [6], Bramwell and Addis [4], Fleischer [10].

Observations on Fraternal Anticipation.

There is some dispute as to the occurrence of fraternal anticipation in mental diseases, i.e. that the disease tends to start at an earlier age in the younger members of a sibship than it does in the elder (A. S. Paterson [18]). As many persons feel perfectly healthy, although showing definite signs of dystrophia myotonica, we cannot always determine the age of onset. At present we can only compare the ages at which persons suffering from dystrophia myotonica began to present symptoms of the disease.

In spite of the numerous families at my disposal, I obtained useful information as to the time of appearance of muscular symptoms in the

following eight families only. In these families 3, 3, 3, 2, 2, 2, 2, and 5 members were definite cases, most of them severely affected. A fraternal anticipation was observed in all, except in the last mentioned (the family S. 2).

(1) Family 8 (a) Klara R., aged 51, feels quite healthy: she had eye trouble at 48 and now presents typical signs of dystrophia myotonica.

(b) Paul B., aged 48: first had trouble in his hands at about 32 and with his eyesight at 46; signs of dystrophia myotonica were typical.

(c) Otto B., aged 34: weakness in his hands started in early infancy and myotonic disturbance in his hands at 8: there was mental enfeeblement for two years. Typical signs of dystrophia myotonica were observed on examination.

(2) Family 6 (a) Mrs. D., aged 58, does not complain of stiffness: she had eye trouble at 52 and an operation for cataract at 56. Definite slight signs of dystrophia myotonica were present in tongue and hands; no wasting was observed but the facial muscles were weak; the knee-jerks were absent.

(b) Robert G., aged 55, noticed loss of power in his lower limbs at 50. Typical myotonia was found in tongue and hands, with slight wasting of the left sternomastoid, forearm and peroneal muscles; the triceps reflex and ankle-jerks were absent: grip was poor. (He died a few months later with carcinoma of the lung.)

(c) Mrs. D., aged 49, had eye trouble at 46 and an operation for cataract at 49; she began to fall when walking and complained of weakness in the hands at 45; there was typical myotonia in tongue and hands; the sternomastoids were completely wasted and the thenars slightly; the upper and lower limbs were weak and she could only walk supported by others.

(3) (a) John McD., aged 26, felt stiffness in his hand at about 20: he had typical signs of dystrophia myotonica.

(b) Albert McD. (died at 17), noticed his hands stiff, probably for the first time at 10; he also had typical signs of dystrophia myotonica at 15.

(c) Eric McD., aged 15, came as a patient to the National Hospital in 1931 at the age of 10; he reported that stiffness started at 8; he had typical signs of dystrophia myotonica.

(4) (a) Irene B., aged 30. Weakness in legs started at 27: a goitre appeared at 26; this was a typical case of dystrophia myotonica.

(b) Cyril B., aged 24, had been mentally defective since infancy: at 24 there were severe signs of dystrophia myotonica.

(5) Family 9 (a) Frank, aged 34, was in good health up to the age of 24; cataract was observed in 1928 and definite sign of muscular disease at 34.

(b) Violet, aged 23, complained of general weakness at 21; walked badly at 20 and had difficulty in learning. She was a typical case of dystrophia myotonica.

(6) (a) J. de N., aged 56, a very severe case of dystrophia myotonica, observed a disturbance of the eyesight at 18 and muscular weakness at 20.

(b) Clara de N., aged 47, a very severe case of dystrophia myotonica, fell down in the street at 10 or 11 and had difficulty in getting up; she could not walk fast six months later.

(7) Family 1. (a) In Frederick T. A. R., aged 50, a severe case of dystrophia myotonica, general weakness started at the age of 30; he was an in-patient at the National Hospital, suffering from severe symptoms, at the age of 36.

(b) John (his step-brother) aged 44, a severe case of dystrophia myotonica, felt stiffness in his hands at the age of 24; he was an in-patient at the National Hospital, suffering with pronounced symptoms at the age of 31.

(8) Family 2 (iii) 8. (a) Charles, the seventh child, who died at 48; complained of weakness at 34.

(b) Letitia, the tenth child, aged 59, felt weakness at 33.

(c) Ellen, the twelfth child, aged 56, noticed weakness at 22.

(d) Laura, the thirteenth child, aged 55, felt weakness in infancy.

(e) Arthur, the fifteenth child, aged 50, noticed weakness at 32.

Thus fraternal anticipation seems to be common, but the number of cases so far available is too small to establish a definite rule.

Heredity of Dystrophia Myotonica.

Nearly all authors agree that dystrophia myotonica is an hereditary affection. My own observations were as follows:—

(1) Cases of dystrophia myotonica in two generations were found in thirteen families which I have examined.

(2) It was reported that one or several members of the preceding generation suffered from dystrophia myotonica in fourteen other families. In some of these families probably members of three or four generations were affected.

(3) In two other families typical cataract was seen in the mothers of patients suffering from dystrophia myotonica.

(4) In nine other families it was stated that a member of the preceding generation suffered from cataract.

(5) In fifteen cases no history of inheritance was available.

Like Boeters [3] I observed half-brothers and half-sisters affected in several families. In the families 1 and 3, the affected persons were descendants of the same father; in the descendants of Mrs. C. (R) 1 (ii) 6, the affected persons were children of the same mother. Percival D. had two affected children by his first wife, while both children by his second wife, both young boys, were suspicious cases.

The frequency with which dystrophia myotonica affects members of two generations as well as the repeatedly observed affection of half-brothers are in favour of dominant heredity.

Evidence in favour of recessive inheritance was observed very rarely

in the families examined. Two patients were the children of first cousins. On the other hand in the family 9 (a) and (b), two men, Simon John T., junior, and Archibald M., were married to cousins of the T. family; but in their children only slightly suspicious signs of dystrophia myotonica were observed. Only one patient reported that both his father and mother suffered from cataract; in all other cases in which a history of cataract in the previous generation was obtained only the father *or* the mother was affected. In one sibship the mother was affected with cataract and had slightly suspicious signs of dystrophia myotonica. More or less suspicious signs were present in relatives of both parents.

TABLE II.

Parents	Children						Total
	U	N	S_1	S_2	A_1	A_2	
U	93 (48%)	4 (2%)	13 (7%)	38 (20%)	19 (10%)	26 (13%)	193
N	15 (42%)	1 (3%)	—	16 (44%)	1 (3%)	3 (8%)	36
S_1	31 (53%)	5 (9%)	1 (2%)	14 (24%)	3 (5%)	4 (7%)	58
S_2	22 (18%)	16 (13%)	25 (21%)	32 (27%)	17 (14%)	8 (7%)	120
A_1	29 (35%)	4 (5%)	2 (2%)	22 (27%)	19 (23%)	6 (7%)	82
A_2	21 (44%)	—	4 (8%)	14 (29%)	4 (8%)	5 (10%)	48

U = not examined.
N = normal.
S_1 = slightly suspicious.
S_2 = suspicious.
A_1 = mildly affected.
A_2 = severely affected.

Dr. L. S. Penrose was kind enough to examine my observations with reference to the relationship of disease in the parent to disease in the children. He drew up Table II and made the following conclusions:—

> "When the parents are normal about 11 per cent. of the children are affected; when the parent has suspicious signs about 16 or 17 per cent. of the children are affected; when a parent is affected about 26 per cent. of the children are affected. If we assume that the majority of the individuals called 'unknown' are normal and that many of the suspicious cases are also normal, this finding would be in keeping with the hypothesis of dominant inheritance, but in which more than one factor is involved. There may be a main 'gene' responsible for myotonia atrophica and numerous modifying influences, one of

which may be associated with birth order. I do not think that the hypothesis of cytoplasmic inheritance which I suggested as a possible explanation of the great variety of forms is very probable, but I think it might be the only way of explaining the extreme rarity of normal individuals."

Fertility.—The number of children born of patients affected with dystrophia myotonica is small. I observed 29 male cases over 23 years of age who had no children. The wives of 18 male cases over 23 years of age had 88 pregnancies, but only 58 children were alive. Twenty-four female cases over 23 years of age had no family. Among 17 female cases over 23 years of age there had been 74 pregnancies; only 39 of the children were alive. Consequently 88 persons affected with dystrophia myotonica had only 97 living children. Among these children a certain number were severely affected mentally, so that they will not marry; other children were affected with "suspicious" signs when young, so that it is doubtful if they will become parents.

The following observations bear on the question whether dystrophia myotonica can be transmitted from previous generations through persons themselves unaffected.

(1) Mrs. L., aged 55, felt perfectly healthy and the only pathological signs I observed were slight wasting of temporals and inability to blow out her cheeks. A brother, who was examined at the National Hospital, was a severe case of dystrophia myotonica. E. G. L., her son, aged 26, presented slight but definite signs of the disease, especially on electrical examination.

(2) Mrs. M. (Family 9 b), aged 74, was healthy and showed no signs of dystrophia myotonica. In many of her children I observed the typical myotonic reaction and slight wasting of muscles. None felt ill or was suffering from dystrophia myotonica. Many cousins suffered from this disease: the father of these cousins was healthy up to his death at the age of 69, but his brother and his brother's son had slight evidence of the disease.

(3) William (2 (ii) 8) (Greenfield [14], 1911), was in good health at the age of 69, when examined by Greenfield. His mother and other relatives suffered from cataract. Many of his children suffered from dystrophia myotonica.

(4) William S. (2 (iii) (8) 3), the son of the above, was normal when examined by Greenfield and never suffered from signs of dystrophia myotonica. In his third child the temporal muscles were wasted, the left sternomastoid was smaller than the right and there was doubtful weakness on blowing out her cheeks.

(5) Sam W. (3 (ii) 18), was normal, but there were signs suspicious of dystrophia myotonica in his three children. His brother, Arthur, was a severe case of this disease.

Although none of these cases was absolutely conclusive, as neither slit-lamp nor electrical examination had been done in the healthy parents, these observations were in favour of a transmission of dystrophia myotonica through healthy persons, as ascertained by Fleischer [10] as well as by Henke and Seeger [15]. This conclusion is at variance with that of those authors who suppose that in dominant inheritance the persons who transmit the affection must themselves be affected.

Familial deterioration.—Fleischer [10] observed progressive deterioration between the fifth and the sixth generation in one branch of a large family, but he believed that it did not come on in the whole family as some branches were in good health. Frey [12] called dystrophia myotonica a heredo-degenerative affection, as he observed progressive deterioration in later generations; the members of these were affected more severely than those of the previous generation. Henke and Seeger [15] found no sign of degeneration in those members of a big family (the same as that examined by Fleischer previously) in whom the "gene" of dystrophia myotonica was not apparent, but they observed progressive deterioration in the affected branches of this family between the fifth and the sixth generations.

In my series of cases the records obtainable were inadequate in fifteen families. Progressive deterioration probably had occurred in eight families in which the father or mother of patients with dystrophia myotonica suffered from cataract, but not from muscular disturbance. In one family 2 (iii) (8) no disturbance was observed by Greenfield in their father, but their paternal grandmother was reported to have had cataract.

I examined two families in whom members of the younger generation suffered from dystrophia myotonica, while their mothers were affected with cataract. One of these mothers was free from other signs; the other mother was affected with slightly suspicious signs of the disease.

Patients suffering from dystrophia myotonica, belonging to fourteen different families, reported that their father or mother had suffered from the disease. We can be sure that the affection started in the parents later than in their offspring as, if not so, they would probably not have married. From three of these fourteen patients a reliable report was obtained that their father had been in good health when he married, and became affected in later life.

Caughey [5] described a family in which probably members of four generations suffered from dystrophia myotonica, and progressive degenera-

tion was evident. I examined two severely affected sisters in the fourth generation of this family who began to suffer at 10 and 20 years of age. Evidently their father had been in good health at that age.

I examined members of different generations in seventeen families in whom those of the second generation became affected at an earlier age and more severely than their parents.

(1) S.-B. (I) The grandmother, aged 85, showed suspicious signs, the muscles of the left thenar eminence being wasted, and probably those of the right thenar also.

(II) The mother, aged 50, showed definite myotonia in the tongue, hypothenar and left thenar muscles, weakness of the facial muscles and wasting of the left temporal and the lateral parts of both thenar groups. On electrical examination tetany was present to the interrupted galvanic current.

(III) The patient, aged 26, had severe myotonia since infancy. There was slight wasting of the temporals and definite wasting of the left sternomastoid. On electrical examination a typical myotonic reaction was observed.

(2) D. (I) The grandmother, aged 76, feels healthy, her left sternomastoid is wasted and left thenar eminence is slightly wasted. Myotonia is present in the left hypothenar muscles: the supinator and triceps reflexes are absent.

(II) In the father (Percival), aged 50 (a brother had suspicious signs), weakness and wasting started at the age of 35; when examined at 50 years of age, he was a typical case of dystrophia myotonica in an advanced stage.

(III) In his son, aged 22 and his daughter, aged 19, definite signs of dystrophia myotonica were found. This son was diagnosed by a psychiatrist as a case of "mild schizophrenia"; in the father Dr. A. S. Paterson observed signs of intellectual degeneration. Two other sons, aged 14 and 11, were suspicious cases.

(3) Mrs. C., aged 59, felt weakness at the age of 40; diabetes was observed at the age of 48. She had severe signs of dystrophia myotonica at the age of 55, although there was certainly no mental disturbance. Of eleven children the eighth was imbecile and physical signs in favour of dystrophia myotonica were observed in infancy (did not laugh). I observed physical signs of dystrophia myotonica at the age of 26. The fourth, fifth and sixth children died in infancy. The first, second, third, and ninth children were not examined. The seventh, tenth and eleventh children showed suspicious signs.

(4) T. (9 (c) (ii) 2). Mrs. G. was operated on for cataract at the age of 46: suspicious signs of myotonia were observed at the age of 48.

Children.—(1) L., aged 24, feels healthy, but has definite myotonia, slight wasting and early cataract.

(2) V., aged 21, felt stiffness at 19; she has now definite myotonia and early cataract.

(3) D., aged 17, complains sometimes of stiffness; she has slight but definite signs of dystrophia myotonica and a suspicion of cataract.

(4) H., aged 14, who complained of stiffness at 13, has slight signs of the disease and early cataract.

(5) F. T. A. R. (1), aged 50, was in the Army at the beginning of the War; at the age of 30, he became weak and was a severe case at 36, when examined in the National Hospital. At 50, Dr. A. S. Paterson reports "memory failing; apt to be depressed, though sometimes cheerful."

Of his eight children the second was not examined; definite signs of dystrophia myotonica were observed in the first, at 28, in the third at 23, in the fourth at 20, in the sixth at 18, in the seventh at 15, in the eighth at 13. In the fifth suspicious physical and severe mental changes were observed at 19. Intelligence was defective in the first, fourth and seventh children.

(6) Mrs. H. (4 (ii) 3), aged 55, noticed a disturbance of eyesight at 31 years, but had no other trouble at that time; she was operated on for cataract at 35. Definite signs of dystrophia myotonica were observed at 54, but there was no grave mental change. Her only daughter was mentally backward from infancy; severe signs of dystrophia myotonica were observed at the age of 29; visual defect started at 10, and she was operated on for cataract at 29.

(7) Mrs. W. (7 (ii) 7), aged 50; visual trouble started at 32, otherwise she felt healthy; she had definite but mild signs of dystrophia myotonica, but no striking mental abnormality; she was able to do her housework.

(*a*) Her first child, aged 23, had suspicious signs of dystrophia myotonica.

(*b*) Her second child, aged 18, had definite changes and attended a special school.

(*c*) Her third pregnancy ended in a miscarriage.

(*d*) Her fourth child was stillborn.

(*e*) Her fifth child, aged 14, who had severe signs of dystrophia myotonica at 13, was mentally defective and in an asylum.

(8) Mrs. D. (6 (ii) 1), aged 58, feels healthy, but has definite signs of dystrophia myotonica; she had trouble with her eyesight at 52 and was operated on for cataract at 56. She was not a brilliant scholar and her memory has failed gradually for some years, but she is still able to do her housework.

She had nine children:—

(1) Son, aged 39, feels healthy but complains of stiffness at times and has suspicious signs of dystrophia myotonica.

(2) Son, not examined.

(3) Son, aged 35, feels healthy, but has definite signs of the disease.

(4) Son, as well as his three children, had suspicious signs.

(5) Son, died at 13.

(6) Daughter, aged 24, had marked signs of dystrophia myotonica and was mentally backward; she left school from the fifth standard at the age of 14.

(7) Son, aged 19, had very marked signs of dystrophia myotonica and was mentally very backward; he left school from the fourth standard at 14.

(8)
(9) } Stillborn twins.

(9) John L. McD., aged 56, felt stiffness in his hands at 20. There were five children with a miscarriage between the third and fourth.

(1) Son, aged 25, is a severe case of dystrophia myotonica: the trouble started at 18 years of age.

(2) Son, aged 23, has suspicious signs of the disease.

(3) Daughter, aged 21, has also suspicious signs.

(4) Son, who died at 17; he had severe dystrophia myotonica at 14 when examined at the National Hospital: these signs started at 10.

(5) Son, aged 14 years, is a severe case of dystrophia myotonica, which started at 8.

(10) Herbert D, aged 53, is a definite case of dystrophia myotonica. The stiffness in his hands started at 37 and he was operated on for cataract at 43.

Ellen, his only child (except an elder boy who died at 3 months), aged 23 when examined, is a definite case of dystrophia myotonica and had been at a special school.

(11) Percy B., aged 53, is a case of dystrophia myotonica; his weakness had started at 36.

He had three children:—

(1) Eldest died at one year of age.

(2) Stillborn.

(3) Daughter, aged 24: is a definite case of dystrophia myotonica; the weakness started at 16 and she is mentally very backward.

(12) Mrs. C. (1 (ii) 6), aged 43, had definite signs of dystrophia myotonica, but felt healthy; mentally she was a little backward but did her housework. She had two children by her first husband.

(1) Son, who died at 6 months.

(2) Daughter, aged 19, is an imbecile, with definite signs of dystrophia myotonica.

There were three children by the second husband.

(3) Son, aged 15, is an idiot, with definite wasting in the sternomastoids; myotonia was not observed.

(4) Son, aged 12, is an idiot, with wasting of the sternomastoids; myotonia was not observed.

(5) Daughter, aged 7, is also an idiot, with some signs of dystrophia myotonica.

(13) James G. (6 (ii) 3), aged 55, is a definite case of dystrophia

myotonica; he lost the power of his legs at 50. He had five children, the four youngest died in infancy.

Ada, the eldest, aged 32, showed definite signs of dystrophia myotonica, although she feels healthy.

(14) Karl B. died at the age of 55. According to the statement of his widow he became affected with signs of dystrophia myotonica after being married; he was in hospital for the first time at 34 years, and was operated on for cataract at 40. His wife had nine miscarriages after the birth of two living sons. The younger, an idiot, was affected with severe dystrophia myotonica.

(15) Paul B. (8 (ii) 2), aged 46, is a definite case of dystrophia myotonica with cataract. After the age of 30 he felt stiffness in his hands, this being the first sign of the disease.

Bernard B., his only son, aged 18, was a definite case of dystrophia myotonica: his mother observed that his voice became affected like his father's when he was 7; he complained of stiffness at 12. His father was a good scholar, but Bernard had difficulty in learning.

(16) Karl S. (12), aged 53, is a definite case of dystrophia myotonica; he had been in the Army for two years.

Willy, his son, aged 24, is also afflicted with the disease and is an imbecile.

(17) Klara R. (8 (ii) 1), aged 51, feels healthy, but had been affected with definite signs of dystrophia myotonica and eye trouble since the age of 48; no mental changes were observed, but a special examination was not made.

Five children.

(1) Daughter, aged 28; a definite case of dystrophia myotonica without mental abnormality.

(2) Daughter, aged 26 and healthy.

(3) Son, aged 25 and healthy.

(4) Son, aged 23 and healthy.

(5) Son, aged 21, a definite case of dystrophia myotonica and an imbecile.

In these seventeen families one or more persons of the "second" generation was a more serious case than his parent, or most probably became affected with dystrophia myotonica at an age at which his parent was in good health. On the other hand, I examined one severe case (Mrs. D. (6 (ii) 5)) aged 50, whose two daughters, aged 27 and 28, as well as two grandchildren, aged 4 and 7½, had only slight symptoms of the disease. Thus while progressive deterioration may occur in some families, it does not seem to be an invariable rule; in some families there may even be a regression in the incidence and severity of the disease.

Mental Deterioration in Later Generations.

It is well known that mental changes occur in a large proportion of patients with dystrophia myotonica. These changes were discussed in a recent paper by Maas and Paterson [17]. Some observations seem to favour progressive deterioration in later generations. I found that almost every patient suffering from dystrophia myotonica in whom mental symptoms were so serious as to need permanent treatment in an asylum, or education in a special school, had a parent who suffered from the disease.

Among the cases which I have observed, twenty had been confined to mental institutions, or had attended special schools for mentally defective children; of these sixteen were definite and four suspicious cases of dystrophia myotonica. In ten instances the father was afflicted with dystrophia myotonica, and in ten the mother. Many other young children of parents with dystrophia myotonica, such as the children of Harcourt and John R. (1) and Arthur W. (3), were mentally backward, while their fathers, though definite cases of dystrophia myotonica, were not much affected mentally.

Several of those cases confined in mental hospitals were the first instances in their families to be diagnosed as cases of dystrophia myotonica, and signs of the disease were later observed in their parents. Further, in many families several brothers and sisters in the parental sibship were examined, so that probably severe mental cases in that sibship would have been found if they had been as numerous in the "first" generation as in the "second" generation.

The fact that I found no "mental" cases in the first generation does not prove that such cases never occur, but my observations indicate that mental disease is at least more common in the later generations of affected families.

Conclusions.

Fifty-seven families in which cases of dystrophia myotonica occurred were examined. Severe symptoms were observed more often in the male sex, while mildly affected and suspicious cases occurred more frequently in the female sex. Probably dystrophia myotonica affects both sexes equally frequently.

A myotonic reaction was more often found on mechanical excitation than on active movements. All striated muscles may exhibit the myotonic reaction.

The cases differ very much with regard to the wasting of muscles. Even in a severe case the facial muscles, the sternomastoids, the supinators or the small hand muscles may remain normal. On the other hand, in some cases the muscles of the shoulder-girdle and of the pelvic-girdle were definitely affected, while other muscles were only slightly atrophied. Weakness was conspicuous in some cases without definite wasting.

Hypertrophy of muscles, or more probably pseudo-hypertrophy, was observed in rare cases.

I did not find one case of pure "Thomsen's disease," but in four patients who had been previously diagnosed as "Thomsen's disease" only a few muscles were wasted. In these four cases cataract was not observed.

The sex glands were affected in the majority of cases, but in two very severe cases their function was preserved.

In many "healthy" relatives suspicious signs of dystrophia myotonica were observed, such as a more or less definite myotonic reaction, more or less definite wasting of facial muscles, sternomastoids or thenar muscles, or weakness of the facial muscles, hands or feet. In the lenses alterations were also observed, which were not definite enough to establish a diagnosis of cataract, but which were suspicious.

Electrical examination seems to be a valuable test in doubtful cases. A typical myotonic reaction was observed in two patients in whom only slightly suspicious signs were revealed by other forms of examination. In many otherwise "suspicious" cases, electrical examination also gave a suspicious result.

Dystrophia myotonica certainly often begins in early childhood. In sibships in which one definite case occurred nearly all the other members were affected either with definite, or with more or less suspicious, signs of the disease.

The younger members of affected sibships were more often severely affected than elder members; in some sibships the most affected was the youngest of male sex, while a younger member of female sex showed less severe symptoms.

My observations were in favour of fraternal anticipation, in the sense that the younger members of the affected sibships become affected at an earlier age.

Dystrophia myotonica often affects the members of succeeding generations; it is transmitted by dominant inheritance. Dr. Penrose supposes that more than one factor is involved.

Dystrophia myotonica may probably be transmitted by persons unaffected with signs of the disease.

The examination for physical signs, and still more the examination for mental changes, in members of succeeding generations demonstrated progressive deterioration in many branches of the affected families.

I am anxious to express my gratitude to all those who have so kindly given me the opportunities to study patients under their care and to those who have aided me by carrying out special examinations.

Most of the slit-lamp examinations were done by Mr. C. Goulden and Mr. T. C. Summers at the London Hospital and the electrical examinations by Dr. L. D. Bailey at the National Hospital. Dr. A. S. Paterson examined numerous cases with regard to their mental states. Dr. L. S. Penrose gave valuable advice with regard to heredity.

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THE EXOGENOUS CELLULAR CONTENT OF THE NEUROHYPOPHYSIS IN MAN UNDER PATHOLOGICAL CONDITIONS.

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THE neurohypophysis, or pars nervosa of the pituitary gland, may be divided from the cellular point of view into endogenous and exogenous parts. The former consists of the cellular elements constantly present in the lobe, such as the pituicytes, whilst the latter comprises those cellular elements which have an origin outside the neurohypophysis and occasionally invade it. These structures are constantly basophil cells which are derived from the pars intermedia and under normal conditions of health may invade the neurohypophysis (*see* [10]). Cushing [1] in 1932 described the syndrome which now bears his name and associated it with a basophil adenoma of the hypophysis. Hypertension is a constant feature of the syndrome and this fact led him to suspect the invading cells as the site of production of vasopressin. However, since 1932, many cases of "Cushing's syndrome" in which obesity, purple abdominal striæ, hypertension, glycosuria, osteoporosis, &c., are prominent features have been reported in the literature, but not all have shown either a basophil adenoma or even an increased basophil content of the neurohypophysis. Post-mortem examinations have in some cases revealed no abnormality, while in others an adrenal tumour has been found. These observations emphasize the close relation between the adrenal gland on the one hand and hypertension and "Cushing's syndrome" on the other. Later (1934) Cushing [2] postulated that in hypertensive states there was an increased basophil invasion of the posterior lobe and that these invading cells were producing vasopressin in larger quantities than normal, as was shown by the raised arterial tension. One criticism that may be levelled at his argument is that we are still in doubt as to the extent to which raised blood-pressure is due to an adrenal and not to a hypophyseal over-activity, for many cases of hypertension, especially the "essential" type, are probably due to the strain of modern life and the consequent sympathetic over-

activity. It will be shown in the present research that Cushing's hypothesis is not substantiated.

Since 1934, many workers including Kraus [6], Berblinger [3], Biggart [4] and Rasmussen [8] have worked on this problem, and while the generally accepted view is that there is no relation between the degree of invasion and the hypertensive states, very little work has been done on the question of a relationship between the basophilic invasion and the pathology of hypertension or other pathological conditions. A histopathological study has been made of this problem by the writer and the histological features, the relation of the invading cells to normal health, &c., and a new method of classification of the degrees of invasion are considered elsewhere [10]. Seventy-five pituitary glands were obtained from post-mortem examinations performed in voluntary and municipal hospitals and by several police surgeons in the area. Seventeen of these were of the "control" class in that they were obtained from cases of street or industrial accident in which there were no pathological conditions.

Four degrees of basophil invasion can be recognized, viz.: Absent invasion (Group 1); slight invasion (Group 2); moderate invasion (Group 3); and extreme invasion (Group 4). Since the storm of pathological discussion has raged around the suggested relationship between the basophil cells in the posterior lobe and the hypertensive states, it is proposed to divide the fifty-eight "pathological" cases into hypertensive, hypotensive and normotensive groups and to compare the findings with the "control" group. Frequent and repeated blood-pressure estimations were performed and those cases whose systolic blood-pressures were over 180 mm. Hg were considered in the "hypertensive" series and a systolic blood-pressure less than 100 mm. Hg was deemed "hypotensive." The "normotensive" group contains all those cases whose systolic blood-pressures were within the generally accepted normal limits for their ages and in whom no vascular pathology was suspected during life or demonstrated at post-mortem examination. The tables show the incidence of basophilic invasion of the neurohypophysis in this series for comparison with the incidence of the invasion in the "control" group.

HYPERTENSIVE SERIES—

Number of cases 28

Group	Number	Per cent.
1	6	21
2	9	32
3	11	40
4	2	7

NORMOTENSIVE SERIES—

Number of cases 28

Group	Number	Per cent.
1	8	28
2	9	32
3	7	25
4	4	15

HYPOTENSIVE SERIES—

Number of cases 2

Group	Number	Per cent.
2	2	100

CONTROL SERIES—

Number of cases 17

Group	Number	Per cent.
1	8	47
2	5	30
3	4	23
4	—	—

These tables show a higher percentage of the Group 1 degree of invasion found in the control glands, equivalent readings are shown in Group 2, with the exception of the two cases of Addison's disease, each of which exhibits a Group 2 invasion which gives a value of 100 per cent. in the hypotensive series. The hypertensive cases show a higher percentage in Group 3 while the normotensive cases have the highest figure in Group 2. The figures are too inconstant for any relationship to be substantiated, for although there is a 16 per cent. increase in the hypertensive states in Group 3, yet in Group 4 there is a deficit of 8 per cent. when each is compared with the normal series. The two cases of Addison's disease in the hypotensive series, insufficient as they are for complete classification, show a Group 2 invasion, whereas if the hypothesis relating height of blood-pressure with the basophil cells were correct, they should exhibit a marked diminution in basophil content. These tables give a graphic picture of the complete absence of any relationship between the basophil cells invading the neurohypophysis and the degree of vascular tension. The cases were further subdivided on more sound pathological grounds and classified according to the pathological condition producing the hypertension. Examples of essential hypertension (confirmed at post-mortem), chronic glomerulonephritis and chronic interstitial nephritis were obtained.

ESSENTIAL HYPERTENSION—

Number of cases 8

Group	Number	Per cent.
1	3	37
2	3	37
3	2	26
4	—	—

The figures in this class are comparable with those in the "control" group and no relationship between the degree of invasion and essential hypertension may be postulated.

CHRONIC GLOMERULO-NEPHRITIS—

Number of cases 4

Group	Number	Per cent.
1	—	—
2	1	25
3	1	25
4	2	50

The most extensive invasion encountered in the series was found in this group. Gland No. 50 from a male, aged 66, with blood-pressure of 290/150 mm. Hg had an invasion greater than Group 4. Systematically higher values are met with in this chronic glomerulo-nephritis class than in any other. The two cases with the Group 4 invasion were 39 and 66 years old respectively, and since the present research has not definitely established a marked increase with age [10], the possibility of a connection between the basophil cells and chronic glomerulo-nephritis is indicated. This is made more forcible when the pathology of the condition is considered. The disease is infective and begins as an acute glomerulo-nephritis, which usually slowly subsides only to be awakened periodically by exacerbations and gradual changes in the kidney substance through the subacute to the chronic stage. This process takes time, in some cases it is more rapid, but the process is usually prolonged over several years and therefore the age factor is less prominent. Hawking [5], Marcano [7], Berblinger [3] and Kraus [6] have made observations that a higher basophil count is seen in such cases.

CHRONIC INTERSTITIAL NEPHRITIS.

This is the group in which one would expect advancing age to play a prominent part, for the renal charges here are secondary to a widespread arterial degeneration, usually atherosclerosis.

Number of cases 15

Group	Number	Per cent.
1	3	20
2	5	—
3	7	47
4	—	—

A considerably higher percentage is found in Group 3 than in the other pathological conditions, and these cases were found on analysis to be responsible for the higher values in the older age classes [7]. The 47 per cent. in this group is more than double that in the control

series and is far higher than that encountered in any table. This affords evidence that the rôle played by the basophil cells in regard to age may be due to cases of chronic interstitial nephritis appearing in those groups. No examples of a Group 4 invasion were met with in this series.

It has been shown that there is no relationship between the invading cells and the height of the blood-pressure or essential hypertension and that chronic glomerulo-nephritis and chronic interstitial nephritis are probably closely related to the degree of invasion. Are these facts capable of correlation? Chronic glomerulo-nephritis and chronic interstitial nephritis have an essential common factor in the renal pathology, a progressive fibrosis. In the former the initial lesion is, broadly speaking, infective and the fibrosis spreads in relation to the glomeruli and tubules, whereas in the latter the disease is degenerative and the fibrosis perivascular and interstitial. In both cases, higher basophil values are encountered. The fact that the blood-pressure is very high in both cases has been shown to be devoid of any relationship. What other factors have these two conditions in common? Glomerulo-nephritis begins as an acute condition involving the capillary loop and tuft in Bowman's capsule and produces desquamation of endothelial cells in that tuft and capsule, considerable exudation and a round-celled infiltration: a true capsulitis and glomerulitis. Interstitial nephritis of the chronic type is produced by the degenerative group of vascular diseases, particularly atherosclerosis, which involve the medium-sized arteries and by diminishing the flow of blood to the kidney produces an interstitial ischæmic fibrosis. In the two conditions the vascular endothelium is involved and it is, therefore, submitted that there is a definite relation between the degree of basophilic invasion and a spreading renal fibrosis, whether infective or degenerative, and that the health of the vascular endothelium plays a separate as well as a collective role.

Cases of tuberculosis and carcinoma, of all types, acute lobar and bronchial pneumonia and syphilis provided sufficient material for investigation and classification. Unfortunately, but seven cases of tuberculosis were obtained, but the figures in Group 3 were nearly double those in the control group, and since all the cases were under 40 years, the issue was not complicated by the age factor. Tolken [9] described a marked invasion in two cases of phthisis in young people. These findings suggest the possibility of a relationship to the degree of invasion in the present research. Such cases usually fall in the younger

age classes and the results therefore are clearer of interpretation. The need for a fuller and more detailed examination of cases of tuberculosis is emphasized and the possibility of tuberculosis having some relation to the basophil cells must at least be recognized until further data is available. No relation could be established between the degree of invasion and carcinoma since all the cases were of the 55 to 80 years class. 67 per cent. had arterial degeneration and 33 per cent. exhibited a concomitant interstitial nephritis. The findings in the pneumonia series compare most accurately with the control series and no relation could be established between the invading cells and the pneumonic process.

Conclusions.

Ninety-three pituitary glands were obtained and 75 subjected to histological examination (serial sections at 10 μ thickness).

No relation could be established between the degree of basophil invasion of the neurohypophysis and "essential hypertension" or the height of arterial blood-pressure.

A relation between the degree of invasion and chronic interstitial nephritis, chronic glomerulo-nephritis and tuberculosis is described.

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HYDROCEPHALIC AND FOCAL CEREBRAL SYMPTOMS IN RELATION TO THROMBOPHLEBITIS OF THE DURAL SINUSES AND CEREBRAL VEINS.

BY C. P. SYMONDS, M.D.

Hydrocephalus.

In 1931 the writer [30] suggested the title Otitic Hydrocephalus to describe a clinical syndrome associated with otitis media. The salient features of this syndrome were the symptoms of increased intracranial pressure (headache, vomiting and papillœdema) without abscess formation and with spontaneous recovery. He reported three further cases under the same title in 1932 [31]. Garland and Seed [17] reported two cases in 1933. Other cases have been reported by Smith [29], Ersner and Myers [14], and Rabbiner [27]. A case which was seen by the writer has been published by Bradbeer and Gibson [6].

The writer has in addition observed five other cases, of which the following brief reports are presented:—

Case 1.—A boy aged 4.

Five weeks before he was brought to see the writer he had had an acute right otitis media with spontaneous perforation. During the next fortnight he complained of frontal headache and once vomited. No symptoms of mastoid involvement could be discovered.

He then developed a paralysis of the right 6th nerve and was taken to an ophthalmic surgeon, who found bilateral papillœdema.

He was brought by train from Leicester and appeared quite fit after the journey. A few days before this a lumbar puncture had been done and gave a clear fluid with no increase of cells or protein. The 6th nerve palsy had already cleared up. He showed 2D swelling of the right disc and 4D of the left, with a number of hæmorrhages on both sides.

Without further treatment the condition of the discs very gradually improved. Seven months later the ophthalmic surgeon reported them normal with full fields and unimpaired visual acuity.

Case 2.—A girl aged 15.

In August, 1932, she had an acute right otitis media. Three weeks after the onset a mastoid operation was done. Five weeks after the onset the right lateral sinus was found thrombosed and the jugular vein tied.

Subsequently she improved and appeared well until a fortnight after the

lateral sinus operation she vomited, complained of diplopia, and was found to have a right 6th nerve palsy and bilateral papillœdema. Lumbar puncture showed a pressure of 280. The fluid contained no excess of cells or protein.

The papillœdema continued to increase up to 3D on each side with many hæmorrhages.

Lumbar puncture was repeated until the pressure reading was found to be normal. Simultaneously the papillœdema began rapidly to subside. Her discs became normal with normal visual acuity.

Case 3.—A woman aged 21.

She had acute right otitis media at the end of May, 1932. A mastoid operation was performed ten days later. Subsequently she developed headache and vomiting.

On June 23 she was found to have advanced papillœdema with hæmorrhages and exudate. Lumbar puncture showed a pressure of over 300 with a normal fluid. Next day the initial pressure was 270. On compression of the right jugular it rose to 308. On compression of the left jugular exactly the same rise was observed. The observation was repeated several times with consistent results.

This patient made an uneventful recovery after treatment by repeated lumbar puncture.

Case 4.—A boy aged 15. He was admitted to hospital on August 2, 1933, with four days' history of right earache. Paracentesis gave a discharge of pus.

On August 6 his temperature rose to 104° F. The mastoid was opened and found to contain pus. There was an extradural abscess and the lateral sinus was covered with granulations.

On August 9 he had a rigor. The right internal jugular was tied. The lateral sinus was found to be pulsating. The cerebrospinal fluid was clear and contained no excess of cells or protein.

On August 14 his temperature was still high, and he complained of headache. He showed 2D swelling of the right optic disc and early swelling of the left.

On August 19 the swelling had increased to 4D on the right and 2D on the left and there were hæmorrhages in both fundi.

He was mentally alert on both occasions. No other abnormal signs were found in the nervous system.

He developed an abscess in the neighbourhood of the right sacro-iliac joint, which was drained. On this account further lumbar puncture was thought inadvisable.

His condition gradually improved and the papillœdema subsided.

Seen four years later he reported himself in good health. The discs were normal and visual acuity full.

Case 5.—A girl aged 8. She was admitted to hospital on October 23, 1933, with a ten-day history of left otitis media. Cortical mastoidectomy was

performed at once. There was a secondary rise of temperature after the operation, and the wound failed to heal.

On December 23, 1933, the wound was re-sutured.

On January 6, 1934, she complained of headache and vomited.

On January 27, there was early papillœdema. The cerebrospinal fluid showed a pressure of 300 mm. with 3 lymphocytes per c.mm. and protein 10 mgm.

On February 1 she had a rigor, followed by a swinging temperature for the next twelve days. Neurological examination showed an increase in the papillœdema on February 1. On February 11 it was beginning to subside.

Lumbar puncture was performed on several occasions. The cerebrospinal fluid, apart from a high pressure, never showed any abnormality.

On February 11 both plantar responses were extensor. No other abnormal signs were observed at any time except the papillœdema.

On March 7 the temperature had been normal for a fortnight. There was slight swelling of the nasal edge of both discs.

Complete recovery ensued.

In discussing the ætiology and pathology of this condition the writer [30] suggested that it was due either to an excessive secretion from the choroid plexus or defective absorption from the arachnoid villi. The possibility of an obstructive internal hydrocephalus from inflammatory swelling or exudate was considered, but was thought to be unlikely owing to the large volumes of cerebrospinal fluid obtained on repeated lumbar puncture. This conclusion has been confirmed by subsequent observations. Moreover, in this syndrome the residual pressure of the cerebrospinal fluid after withdrawal of 15 to 20 c.c. is relatively high, a point which is against the theory of an obstructive hydrocephalus.

A fact which has engaged the attention of several observers who have written about these cases is the high proportion in which there has been an associated thrombosis of the lateral sinus on the side of the affected ear. It has, in fact, been suggested that obstruction of the lateral sinus may in itself be responsible for the increased intracranial pressure. Against this, however, it is to be observed, first, that lateral sinus thrombosis with otitis media is relatively common, and hydrocephalus rare. The lateral sinus, therefore, is very often thrombosed without hydrocephalus. Second, otitic hydrocephalus may occur when, as judged by the Queckenstedt test, both lateral sinuses are patent, as in the writer's Case 3, above, and in Garland and Seed's Case 2.

The incidence of lateral sinus thrombosis is, however, so high in otitic hydrocephalus that it must have some important bearing upon the problem of ætiology. In the twelve cases seen by the writer

thrombosis was proved at operation in five: in two others preceding the hydrocephalic symptoms there had been a rigor followed by a period of swinging temperature; and in another there had been an attack of shivering, followed ten days later by pain and stiffness in the neck on the side of the affected ear. Thus, in five cases lateral sinus thrombosis was proved, and in another three it was probable.

It would appear then that *infection* of the lateral sinus plays an important part in the causation of otitic hydrocephalus, but that *obstruction* of the lateral sinus is not the essential factor.

The possibility next to be considered is that of a thrombo-phlebitis beginning in the lateral sinus and extending by mural spread, but not necessarily with obstruction, up to the torcular with extension to, and thrombosis of, the straight sinus. Resulting from this, engorgement of the choroid plexuses might occur with consequent over-production of cerebrospinal fluid. This hypothesis is invalidated by the experimental observations of Bedford [3, 4], who found it impossible to produce hydrocephalus in the dog or monkey by occlusion of the great vein of Galen.

The remaining possibility is that, with or without obstruction of the lateral sinus, a mural thrombo-phlebitis might spread up into the superior longitudinal sinus and interfere with absorption of the cerebrospinal fluid through the arachnoid villi. These outlets for the flow of cerebrospinal fluid from the subarachnoid space into the venous sinuses are, according to Weed [32], most numerous and most highly developed in the walls of the superior longitudinal sinus, especially in the area in which the large superior cerebral veins enter this sinus.

Out of this two questions arise: Can retrograde thrombo-phlebitis extend from the lateral into the superior longitudinal sinus? Is it possible that thrombosis of the superior longitudinal sinus may produce the symptoms of hydrocephalus and none other? Both these questions can be answered in the affirmative.

Nielsen and Courville [24] report post-mortem observations in forty-three cases of lateral sinus thrombosis associated with otitis media. In six of these the thrombosis had extended into the superior longitudinal sinus. In five of these cases both mastoids were infected and both lateral sinuses thrombosed. In one case the right mastoid and right lateral sinus only were infected.

Bailey and Hass [2], reporting a case of right otitis media with thrombo-phlebitis of the right lateral and superior longitudinal sinuses, accept otitis media (with or without mastoiditis), lateral sinus throm-

bosis, and retrograde propagation of the thrombus into the superior longitudinal sinus, as a well-recognized sequence.

Their case also provides an example of superior longitudinal sinus thrombosis causing hydrocephalic symptoms only. The patient, aged 6, following right otitis media, showed papilloedema, with a cerebrospinal fluid pressure of 250 mm. The fluid contained 200 red blood-cells and 30 white blood-cells per c.mm. and the total protein was 30 mg. per cent. The papilloedema receded before death, which was due to cardiac failure with mitral stenosis.

Post-mortem adherent thrombi were found from the right sigmoid sinus up to the torcular and thence along the superior longitudinal sinus to include its middle third. At no point could complete occlusion of any of the sinuses be demonstrated. Microscopic examination showed organization and canalization of the thrombi, which occupied about one half the lumen in each sinus.

It is suggested that this case may be taken as an example of otitic hydrocephalus with post-mortem evidence, not only of its cause, but of the process of organization and canalization of the clot, which, as a rule, ends in complete recovery. Had the patient not died of his heart disease we may suppose that he might have recovered from the symptoms of hydrocephalus which were already receding.

Two other cases have been published recently of proved thrombosis of the superior longitudinal sinus with symptoms of hydrocephalus. Frenckner's case [16] was that of a girl, aged 17, who had a chronic suppurative otitis media (side not mentioned). Radical mastoidectomy was performed, but the ear continued to discharge. Six weeks after the operation she complained of headache and diplopia, and two weeks after this was found to have bilateral papilloedema. There was no clinical evidence of brain abscess. The cerebrospinal fluid pressure was 350 mm.

Frenckner, suspecting lateral sinus thrombosis, attempted a sinogram by the injection of perabrodil into the superior longitudinal sinus through a drill hole 5 cm. above the external occipital protuberance, following a technique employed by him since 1934 [15]. In this instance, although X-rays showed his cannula to be correctly inserted into the sinus, he could obtain no blood. Subsequently an opaque injection into the internal carotid enabled him to obtain a phlebogram, which showed obstruction of the superior longitudinal sinus from approximately the level of the parietal eminence back to the torcular.

Four months later the patient was subjectively and objectively well,

except that bilateral papillœdema was still present. The clinical story of this case is that of otitic hydrocephalus.

In a case recorded by Ellis [13] and seen by the writer, the origin of the infection was not in the middle ear, but in an infected umbilical vein. There were thrombosed veins over the left tibia and left chest, followed by a gradual enlargement of the head. This was associated with optic atrophy and mental dulness.

Ventriculography showed extreme dilatation of the ventricular system. Injection of perabrodil into the longitudinal sinus showed a complete block about 2½ in. posterior to the anterior fontanelle.

Dr. Ellis informs me that at the time of writing—eight months since the publication of his report—there has been no further enlargement of the head, and the child's mental condition is improving.

What at first appears remarkable in these three cases of proved thrombosis of the superior longitudinal sinus is that none of them showed any of the symptoms commonly associated in the mind of the clinician with this state, for instance, unilateral or bilateral convulsions, hemiplegia or diplegia. Nielsen and Courville [24] have noted the variability, and in some cases the absence, of symptoms in cases of superior longitudinal sinus thrombosis from otitis media, and conclude that this sinus may be thrombosed, if not infected, without causing any serious cerebral damage. Probably the rate of onset is an important factor. If the progress from lateral sinus upwards is slow, an adequate collateral circulation may be established for the venous drainage of the cerebral cortex, especially if the anterior part of the sinus remains patent. Under such circumstances the only clinical symptoms might be those due to failure of absorption of the cerebrospinal fluid, with resulting hydrocephalus.

If otitic hydrocephalus is, in fact, the result of a lateral sinus thrombosis spreading upwards into the superior longitudinal sinus, then this complication ought to occur more frequently with infection of the right ear than the left, for the superior longitudinal sinus as a rule is continuous with the right transverse sinus, while the straight sinus is continuous with the left transverse sinus. Poirier and Charpy [26] state that in 50 per cent. of cases at the torcular the longitudinal sinus is directly continuous with one or other lateral sinus and that when this is so in three cases out of four it is continuous with the right lateral sinus. Woodhall [33], in an analysis of 100 consecutive cases, has found a rather higher preponderance of major communication between the superior longitudinal sinus and the right lateral sinus.

It appears, therefore, that the chances of a right, as opposed to a left lateral sinus, thrombosis extending into the superior longitudinal sinus are as about 6 to 4, or 7 to 3. In twenty-six cases of otitic hydrocephalus, including those reported in the present paper, in which the otitis media was unilateral, the right ear was affected in seventeen and the left ear in nine. The number of cases is too small to be of statistical value, but the figures are suggestive.

On the evidence which has been presented the writer believes that the clinical syndrome to which he gave the name otitic hydrocephalus is in fact symptomatic of superior longitudinal (or sagittal) sinus thrombosis.

If the symptoms of hydrocephalus which may be associated with otitis media are caused by thrombosis of the superior longitudinal sinus, the same clinical picture should be seen from time to time in cases of superior longitudinal sinus thrombosis from other causes. Ellis's case, already quoted, provides an example of such an occurrence. The two following cases, though lacking pathological proof, are recorded as probable examples:—

Case 6.—Mrs. S., aged 44, on August 26, 1934, developed a temperature of 100° F. together with enlarged glands behind the angle of her right jaw. These increased in size, and on August 29 an incision was made with the expectation of pus. No pus was found, but a portion of an enlarged gland was removed from the neighbourhood of the right internal jugular vein.

On August 31 she had a rigor, and thenceforward ran a swinging temperature for a week with complaint of severe pain in the back of her neck and the top of her head.

On September 9 papillœdema was observed. Lumbar puncture was performed. The pressure was not measured. The fluid was clear and contained six lymphocytes per c.mm. and 50 mgm. of protein.

On September 11 a suboccipital exploration was performed on the suspicion of an extradural abscess, but none was found.

She was seen by the writer on September 13, who found 3 dioptres of papillœdema on each side, but discovered no other abnormal signs. Apart from continuous and severe neuralgic pain in the right suboccipital region and right side of the head, she had no complaints.

She had a further rigor on September 16, after which, in the course of a week, her temperature became normal.

Subsequently she made a complete recovery.

It is suggested that in this case the right lateral sinus became infected, with thrombo-phlebitis spreading into the superior longitudinal sinus.

For the notes of the next case the writer is indebted to Dr. Hinds Howell, under whose care the patient was admitted to the National Hospital, Queen Square:—

Case 7.—Herbert K., aged 44, in November, 1934, developed pain in the calf of the left leg. Subsequently the leg became swollen and tender. His doctor diagnosed the condition as phlebitis and put him to bed for eight weeks. Pain and swelling gradually subsided and he was allowed up. The symptoms then recurred.

He returned to bed in January, 1935, and began to have headache and vomiting. He was then admitted to hospital, and while in bed woke one morning to find his right leg swollen, shiny and tender like the left.

On February 25 there was a discharge of about 2 oz. of pus per rectum.

With prolonged rest his legs improved, but he continued to suffer from bouts of headache and vomiting at intervals of a week or so. Occasionally he complained of double vision.

He was admitted to the National Hospital on this account on April 4, 1935. On examination he showed bilateral papillœdema of 2 to 3 dioptres. Visual acuity was $\frac{6}{24}$ on the right, $\frac{6}{12}$ (partly) on the left. The left arm-jerks were slightly brisker than the right. There were no other abnormal signs.

The cerebrospinal fluid showed a pressure of 295 and contained 2 lymphocytes per c.mm. and 70 mgm. of protein.

He made a gradual spontaneous recovery.

The story in this case is that of a thrombo-phlebitis migrans, probably secondary to a peri-rectal abscess. It is suggested that the hydrocephalic symptoms were due to thrombo-phlebitis of the superior longitudinal sinus.

McAlpine [20] has recorded under the title of toxic hydrocephalus five cases in which he suggests that nasopharyngeal infection was the causal factor. In one of these cases the signs of Hodgkin's disease developed later with enlarged glands on the left side of the neck. This raises the possibility of lateral sinus thrombosis on that side. In none of the other four cases were there any symptoms to suggest the possibility of thrombo-phlebitis.

Goldman [18] regards infection spreading from the throat as a not very uncommon cause of thrombo-phlebitis of the jugular bulb and lateral sinus. The primary cause may be an insignificant sore throat or an abscess in the vicinity of the tonsils. A latent period may follow a tonsillar infection, and varies from a few days up to even four weeks. Maybaum [21] confirms these observations and states that a retrograde spread may take place over a considerable extent even to the dural sinuses on the opposite side without being recognized clinically. During

the course of a retrograde thrombo-phlebitis there may be for a considerable interval complete cessation of evidence of sepsis.

In only one of McAlpine's cases, however, was there a history of sore throat before the onset of hydrocephalic symptoms, and in none was there any fever or constitutional disturbance. There is, therefore, no evidence in favour of the assumption that his cases are related to the group at present under discussion.

Focal Epilepsy and Hemiplegia.

Passot [25], who first clearly described the clinical syndrome since named otitic hydrocephalus, drew attention to a separate cerebral complication of otitis media, which he thus described. After a brief phase of headache and drowsiness there is a sudden onset of Jacksonian convulsions: these may be facial, facio-brachial or facio-brachio-crural. Sometimes monoplegia or hemiplegia may occur suddenly without convulsions. He recorded several such cases in which exploratory operation on the affected side of the brain resulted in a gush of clear fluid from the lateral ventricle with subsequent recovery.

Many cases of this kind have been recorded with spontaneous recovery. Chalier and Naussac [10] in 1931 reported an example with post-mortem investigation. The patient, aged 6½ years, was admitted to hospital on April 25 with scarlet fever and subsequently contracted diphtheria. On May 17 there was a sero-purulent discharge from the right ear. There was no rise of temperature nor any clinical evidence of mastoiditis. On May 22 there was a convulsive attack of the Jacksonian type affecting the left limbs. An hour later there was a generalized epileptic attack followed by coma, and death within a few hours.

At post-mortem the superficial cerebral veins were found to be engorged and in some areas thrombosed, with hæmorrhagic infarction of the surrounding brain substance. The superior longitudinal sinus contained ante-mortem clots adherent to its wall especially in the segments corresponding with the areas of infarction. The right lateral sinus also was thrombosed.

The writers comment upon the dramatic onset of cerebral symptoms, without any warning signs suggestive of sinus thrombosis. They refer to other cases with rapidly progressive hemiplegia without convulsions, in one of which (following an operation for carcinoma of the maxillary antrum) the post-mortem findings were the same as in the case quoted above. They conclude that Jacksonian epilepsy or hemiplegia of rapid

onset may be the first evidence of a thrombo-phlebitis of the superior longitudinal sinus.

Courville and Nielsen [12] have revived interest in this subject. After reviewing the literature, they record briefly twenty-three personal observations of sudden hemiplegia, with or without convulsions, occurring in infants or young children with otitis media. In twelve instances complete spontaneous recovery ensued in from one to forty days. In one case an abscess was found in the left parietal lobe and was drained successfully. In this and four other cases recovery from the hemiplegia was incomplete. There were six deaths, two from generalized meningitis. The post-mortem data were meagre, but the authors conclude from the abrupt onset of symptoms that the primary lesion is vascular, and venous rather than arterial. They believe that the pathway of infection is by way of the small veins draining the middle ear and antrum, thence into the local dural veins, and ultimately by way of the lateral sinus, or the superior petrosal sinus, into the inferior anastomotic vein (vein of Labbé) which opens at one end into the genu of the lateral sinus and at the other into the superficial middle cerebral vein. "The absence of valves in the venous channels, the comparative sluggishness of the blood flow and the easy reversibility of the current incident to coughing, sneezing, and so on, may well account for the distant localization of an embolus, infected or otherwise." As the result of this there may occur a local non-suppurative inflammatory reaction, or thrombosis leading to an infarction. The latter may become infected and give rise to an abscess. Meningitis may develop from the embolic lesion and may be circumscribed or diffuse.

In other papers the same writers [11, 23, 24] emphasize the importance of thrombo-phlebitis of the lateral sinus as a stage in the development of the focal lesion which causes hemiplegia. From the lateral sinus thrombosis may spread directly to the parietal cortex by way of the inferior anastomotic vein, or it may extend into the superior longitudinal sinus and thence into one or other of the tributaries which drain the dorso-lateral surface of the brain. In either case the thrombosed vein in its passage between dural sinus and cortex must traverse the subdural and subarachnoid spaces. If the thrombus is infected a subdural abscess, or lepto-meningitis may develop. Thrombosis of the superior longitudinal sinus itself, they believe, may occur without any symptoms of serious cerebral damage so long as there is no spread into its tributaries.

Byers and Hass [7] report the post-mortem findings in fifty cases

of thrombosis of the dural venous sinuses in infancy and in childhood together with some clinical observations. They conclude that in thrombosis of the superior longitudinal sinus the patient may die without any suggestive symptoms unless the middle superior veins are obstructed. If this occurs convulsions result, sudden in onset and limited to one side of the body. Often after recurrence they become generalized. In these cases small hæmorrhages were found in the meninges and focal hæmorrhagic necroses in the cerebral cortex. If the middle superior cerebral vein on both sides was obstructed, these lesions were bilateral.

Bailey and Hass [2], in reporting three cases of superior longitudinal sinus thrombosis with post-mortem evidence, discuss the possibility of recovery by means of organization and canalization of the thrombi, and emphasize the importance of the intracerebral necroses and hæmorrhages as a cause of subsequent Jacksonian epilepsy in such cases.

It is impossible to be certain of the pathology in the case of patients who recover, but from the data reviewed it would seem at least possible that the sudden appearance of focal symptoms—Jacksonian epilepsy or hemiplegia—in otitis media is due to thrombo-phlebitis in the cerebral veins, which may have spread from the ear along either of the channels mentioned. This hypothesis is in accord with the post-mortem findings in a few fatal cases. In the patients who survive it supplies an explanation both for the rapidity of onset and the mechanism of recovery. It explains also the inconstant association of this syndrome with meningitis, subdural abscess and cerebral abscess.

The writer has notes of seven of these cases, but with no opportunity, for a complete post-mortem examination. One patient died after a subdural abscess had been opened; the others recovered either completely or with slight residual hemiparesis. Two examples may be briefly recorded for the sake of illustration :—

Case 8.—Eric P., aged 2, was admitted to Guy's Hospital under Mr. Layton, on June 22, 1936, with right otitis media of some days duration. At 10 a.m. on that day he began to have left-sided convulsions, continuing without interruption until 3 p.m. At 6 p.m. he showed a flaccid left hemiplegia. His temperature was 103° F.

The writer saw him next day at 10.30 a.m. He was awake but dazed and did not recognize his mother. There was weakness but no paralysis of the left limbs, and the left plantar response was extensor. Lumbar puncture gave a clear fluid containing 600 cells per c.mm. of which 45 per cent. were polymorphonuclear. The protein content was 30 mgm.

Cortical mastoidectomy was performed the same day. Pus was found.

After this the temperature fell gradually to normal, and on the fourth day after operation the child was alert and eating well and showed no abnormal physical signs.

Case 9.—Bernard R., aged 15, was admitted to the Central London Hospital under Mr. Archer Ryland, on November 22, 1929. He had had a discharging left ear for three years. For three days he had complained of pain behind the left ear and his temperature had been raised.

On November 25 left cortical mastoidectomy was performed. After the operation the temperature remained high, and on December 12 there was complaint of headache. Slight neck stiffness was observed and lumbar puncture gave a hazy fluid. Two days later the wound was reopened. The dura appeared healthy and was not incised.

On December 17, in the course of a few hours, he developed a right hemiplegia with dysphasia. The cerebrospinal fluid contained 1,570 cells per c.mm. of which 35 per cent. were polymorphonuclears. The wound was reopened. The dura again was found to be healthy in appearance though abnormally tense. It was not incised but an exploratory needle was inserted through it into the brain in three different directions. No pus was obtained.

The patient remained hemiplegic for six days, and then for the first time had a series of right-sided convulsions.

Subsequently he made a gradual recovery, and was discharged from hospital on June 10, 1930, with a slight residual hemiparesis.

Transient symptoms of a cerebral lesion may also occur in association with thrombo-phlebitis in other parts of the body. Ryle [28], in a case of thrombo-phlebitis migrans, records an episode of vomiting with a sensation of stiffness in the left face and a "woolly" feeling in the left hand, which he attributed to involvement of a cerebral vein.

The following case provides an example of extensive thrombo-phlebitis of the dural sinuses and cerebral veins resulting from puerperal infection :—

Case 10.—Mrs. B., aged 28, was seen by the writer on May 2, 1934. She had passed through her first pregnancy without event save for a mild attack of pyelitis, and on April 13 had been delivered of a healthy child. Towards the end of the first week after the confinement she complained a good deal of headache.

On April 21 she complained of a sudden præcordial pain with a sense of suffocation. Shortly after this she passed a large clot *per vaginam* and other clots during the next day or two. During these days there was complaint of severe frontal headache.

On April 30 headache was very severe and was associated with vomiting. On this day she first complained of weakness of the left arm, and became drowsy and confused

When examined on May 2 she was lethargic. Her temperature, which had not previously been raised, was 100° F. There was evident weakness of the right lower face, and of the left upper limb. Both lower limbs were a little spastic, and both plantar responses were extensor. No other abnormal signs were discovered.

Lumbar puncture had already been performed. The pressure was not measured. The fluid was slightly bloodstained and contained no excess of white cells. The protein was 55 mgm.

She was admitted to Guy's Hospital on May 4. She was then much more drowsy and showed a left hemiparesis. Lumbar puncture showed a pressure of 130 mm. Pressure upon the left jugular vein caused a rise to 160 mm.: upon the right a rise to 190 mm. Bilateral jugular compression caused a rise to 280 mm. The residual pressure after withdrawal of 4 c.c. was 70 mm. The cerebrospinal fluid was bloodstained and yellow. It contained 2,000 red cells per c.mm. On standing there was no clot formation and the supernatant fluid was golden yellow. During the next day the left hemiplegia became complete and was accompanied by sensory loss and left homonymous hemianopia. The temperature rose to 102° F.

On May 5 exploratory craniotomy was performed over the right parietal area. The superficial cerebral veins were found greatly engorged.

She died in coma on May 7. At post-mortem extensive patchy thrombophlebitis was found affecting the superior longitudinal sinus, both lateral sinuses and the superficial cerebral veins. There were several small subcortical hæmorrhages the size of a cherry. Microscopic examination showed mural thrombi of varying age in the sinuses, obstructing the lumen. The oldest thrombi were found in the superior longitudinal sinus. In some of these the process of organization was well advanced and canalization was evident. Over the right hemisphere the superficial veins were completely occluded, and the underlying brain substance showed scattered and diffuse areas of hæmorrhagic necrosis.

Hydrocephalic and Focal Symptoms in the same Case.

It has been suggested in the first section of this paper that hydrocephalic symptoms developing in a patient with an infective focus in the neighbourhood of one of the dural sinuses, or in association with thrombo-phlebitis elsewhere in the body, may be due to thrombophlebitis of the superior longitudinal sinus, and that organization of the thrombi may lead to recovery. In the second section it has been suggested that focal symptoms occurring under like conditions may be due to thrombo-phlebitis in the cerebral veins, and that this may in some instances have spread from the superior longitudinal sinus. In such an instance, if the patient lived long enough, one might expect to observe hydrocephalic and focal symptoms together. The writer believes that the following case provides an example of this association :—

Case 11.—L. B., aged 19, a recruit in the Royal Air Force, was admitted to the National Hospital, Queen Square, on April 20, 1936, at the instance of Wing-Commander Burton.

On March 20, 1936, he complained of sore throat.

On March 26 he was admitted to his local hospital with a right-sided peritonsillar abscess and a temperature of 103° F.

On April 4 the abscess burst, but his temperature did not fall to normal until April 11.

On April 12 he was first allowed up, and while he was having his tea his left arm became dead and weak. He could not move the hand properly and had poor movement at the elbow. During the evening the weakness increased. He woke next morning to find the arm powerless and also noticed weakness of the left face.

On April 16 he had a sudden severe pain across the back of the neck, and subsequently had a rigor.

On April 18 lumbar puncture was performed. The pressure was 250 mm. The cerebrospinal fluid was clear and colourless, contained 3 lymphocytes per c.mm. and 50 mgm. of protein. The white blood-count on the same day was 32,600, and 77 per cent. of the cells were polymorphonuclear.

From April 16 onwards until admission, his evening temperature varied from 102° to 104°.

On admission he complained of pain and stiffness in his neck. Movement was restricted in all directions, and was painful. He was tender over the mid-cervical spine and over the muscles on each side of the neck. There was gross left facial weakness and flaccid paralysis of the left upper limb. The left plantar response was occasionally extensor. No other abnormal signs were detected.

On April 22 the cerebrospinal fluid showed a pressure of 220 mm. There was an adequate rise of pressure with jugular compression on either side, but that on the right was slower than that on the left. The fluid contained no cells. The protein content was 35 mgm.

On April 23 there was some return of power at left shoulder and elbow, and from this time onwards the weakness both of face and upper limb showed steady improvement, so that on June 19 power in the two arms was equal and there was a slight weakness only of the left face.

Meanwhile, however, on May 5 early papilloedema was noted, and he began to have morning headaches.

On May 20 there were two dioptres of swelling in each eye with exudate spreading out into the retina.

On May 26 the cerebrospinal fluid pressure was 300 mm., and the residual pressure, after removal of 5 c.c., was 260 mm. The fluid contained 1 lymphocyte per c.mm. and 40 mgm. of protein.

From this date onwards lumbar puncture was performed every third day. The initial pressure was recorded and enough fluid removed to bring it down to a normal or subnormal level. At first it was necessary to run off 20 to

25 c.c. of fluid to obtain the required fall of pressure. Under this treatment headache disappeared, and the papillœdema gradually subsided.

On July 17 the cerebrospinal fluid showed a pressure of 150 mm., which fell to 60 mm. after withdrawal of 20 c.c., and lumbar puncture was discontinued.

The cerebrospinal fluid was frequently examined, and found normal on every occasion.

He was discharged from hospital on July 29. His discs then showed no swelling, visual acuity was $\frac{6}{9}$ in each eye, and there was no residual trace of the brachio-facial monoplegia.

The sequence of events in this case suggests a thrombo-phlebitis of the right lateral sinus, arising from the peritonsillar abscess, which spread to the superior longitudinal sinus, and thence into one of its tributaries draining the right pre-central cortex. It must be presumed that the right lateral sinus was infected but not obstructed. (The initial observation of a slow rise of cerebrospinal fluid on right jugular compression suggests a partial obstruction at that time.) Anoxæmia rather than necrosis must have been the basis of the paralytic symptoms, from which recovery was so rapid and complete. The process of recovery generally must have depended upon organization and canalization of the thrombi.

In connection with the original site of infection in this case, it is interesting to record Goldman's [18] opinion that "an important factor in the production of a phlebitis of the internal jugular vein is the presence of an abscess in the vicinity of the tonsil."

The Cerebrospinal Fluid in Intracranial Thrombophlebitis.

In lateral sinus thrombosis secondary to otitis media the cerebrospinal fluid is, as a rule, clear and colourless, with no excess of cells or protein.

Sometimes there is associated with lateral sinus thrombosis clinical evidence of meningitis with appropriate findings in the cerebrospinal fluid. These cases need not be discussed further. Between these extremes there are a number of cases in which the clinical signs of meningitis are lacking, but the cerebrospinal fluid shows an increase of cells and a small increase of protein.

Carmichael [9] records seven examinations of the cerebrospinal fluid in six cases of lateral sinus thrombosis from otitis media, three of them fatal. In five instances the cell count varied from 4 to 7 cells per c.mm. In three of these fluids one or two of the cells were polymorphonuclear. In one case there were 16 cells per c.mm., all lymphocytes, and in the other 50 cells per c.mm. of which 5 were polymorphonuclear. The protein content varied from 10 to 45 mgm.

Byers and Hass [7] in a review of 50 cases of fatal thrombosis of the dural sinuses in infancy and childhood report the examination of the cerebrospinal fluid in twenty-nine instances. They divide their cases into a group in which the cause was presumably infective and a group in which the thrombosis was "primary." In all the cases of the "primary" group and apparently in most of the infective group the superior longitudinal sinus was involved, and in many cases the lateral sinuses and cerebral veins. In the infective group 12 cases showed frank meningitis with corresponding changes in the cerebrospinal fluid. In one case there were 13 polymorphonuclear cells, and in another a xanthrochromic fluid. In the "primary" group only two cases showed a normal cerebrospinal fluid. In these two instances the thrombi proved to be of mural type, and did not obstruct the venous channels. In the others the cell-count varied from 4 to 960 cells per c.mm. The usual finding was from 10 to 30 cells per c.mm. and the proportion of polymorphonuclears varied from 30 per cent. to 80 per cent. In the "primary" group the presence of red blood-cells was common: in two cases grossly bloody fluid was found and in three a xanthrochromic fluid.

In Bailey and Hass's [2] Case 1, with thrombosis of the right lateral sinus spreading up into the superior longitudinal sinus the cerebrospinal fluid was clear and contained 200 red and 30 white blood-cells with a protein of 30 mgm. In their Case 2 there were 608 red and 12 white blood-cells. In this case there was a subdural hæmatoma. In their third case with thrombosis of the superior longitudinal sinus there was evidence of recent subarachnoid hæmorrhage with corresponding changes in the cerebrospinal fluid.

In Ellis' case [13] the cerebrospinal fluid at first showed the presence of old blood, but was clear two weeks later after repeated lumbar puncture. In Case 10 of the present paper the cerebrospinal fluid was at first normal, save that it was slightly blood-stained. Later it was frankly bloody with a xanthrochromic supernatant fluid on standing.

In otitic hydrocephalus the cerebrospinal fluid is, as a rule, reported normal. In some cases, however, the development of the characteristic clinical picture has been preceded by frank meningitis as in Symonds' [30] Cases 1 and 3; and in others by a transient meningeal reaction as in Mygind's [22] Case 2. In this case on the first day of observation with a pressure of 400 mm. the cerebrospinal fluid contained 26 lymphocytes per c.mm. The cell count gradually fell till on the sixteenth day,

when headache, vomiting and papillœdema were associated with a pressure of 950 mm., there was 1 lymphocyte per c.mm. Garland and Seed's [17] Case 2 is exceptional, in that throughout the whole course of the illness the cerebrospinal fluid showed a cell count of from 6 to 450 per c.mm., which in the early stages consisted chiefly of polymorphonuclears.

In the cases with hydrocephalic symptoms reported in this paper, in which the cause was other than otitis media, the cerebrospinal fluid was normal.

In the group of cases with focal epilepsy or hemiplegia collected by Courville and Nielsen [12] the cerebrospinal fluid was examined in 7 cases and was normal in 5. One showed 21 cells per c.mm., mostly polymorphonuclears, another 12 lymphocytes per c.mm. In the writer's cases belonging to this group the cerebrospinal fluid was examined in four instances in addition to Cases 8 and 9 of this paper. In one the cerebrospinal fluid was normal; one showed 360 cells per c.mm., mostly polymorphonuclears; the other two showed a slight pleocytosis in which the majority of cells were lymphocytes.

One may conclude from these data that the findings in the cerebrospinal fluid in proved cases of intracranial thrombophlebitis are variable. Fatal occlusion of the superior longitudinal sinus, as a rule, leads to the appearance of red blood-cells in the cerebrospinal fluid, and sometimes to the typical picture of subarachnoid hæmorrhage. Mural thrombosis in this sinus without occlusion may occur with a normal cerebrospinal fluid.

An inflammatory type of reaction may be found in the cerebrospinal fluid with superior longitudinal sinus thrombosis of supposedly non-infective origin.

In the infective cases the cerebrospinal fluid may be normal, or there may be any degree of meningitis, from a clear fluid with a lymphocytic pleocytosis to a hazy fluid with a high proportion of polymorphonuclears. The variability in this group may depend upon several factors, including the degree of infection of the thrombi, and the depth to which the wall of the sinus is involved. The possibility of an associated meningitis by direct spread from the original focus of infection has also to be considered.

Turning to the cases in which the diagnosis of thrombo-phlebitis was non-proven, in the group with hydrocephalic symptoms, we find that the cerebrospinal fluid is almost always normal. The development of hydrocephalic symptoms may be preceded by a more or less severe

meningeal reaction, and in one case, that of Garland and Seed, the increase of cells and protein persisted and was associated with the hydrocephalic symptoms.

There is a discrepancy here between the frequent presence of blood in the cerebrospinal fluid in cases of proved thrombosis of the superior longitudinal sinus, and its absence in the cases of otitic or infective hydrocephalus in which the writer has suggested thrombosis of that sinus as the cause. It is possible, however, that this discrepancy may depend upon the fact that in the former group, with the exception of two cases, the proof of superior longitudinal sinus thrombosis was obtained only at post-mortem. In the fatal cases with extensive occlusion of the sinus there is nearly always occlusion, if not thrombosis, of the large, middle group of superior cerebral veins, and with this often subarachnoid hæmorrhage, and areas of red softening in the brain. The degree, extent, and localization of thrombosis in the superior longitudinal sinus resulting in a bloodstained cerebrospinal fluid, may be those which usually result in death before hydrocephalic symptoms have had time to appear.

The cases in which proof of superior longitudinal sinus thrombosis was obtained in patients presenting hydrocephalic symptoms who recovered are those of Ellis [13] in which blood was found, and Frenckner [16] in which the pressure of the cerebrospinal fluid is recorded at 350 mm. but no mention is made of its examination. One may assume that it was not grossly bloodstained. In this case, as recorded by the phlebogram, only the posterior part of the sinus was occluded.

In the group of cases with focal epilepsy or hemiplegia ending in recovery the cerebrospinal fluid may be normal, but in about half the cases there is a pleocytosis. This is in marked contrast with the hydrocephalic cases, in which the fluid is almost always normal. The difference may be explained by the assumption that an infected thrombus in a thin-walled cerebral vein is more likely to provoke a meningeal reaction than a similar thrombus in one of the thick-walled dural sinuses.

Summary and Conclusions.

(1) The clinical syndrome of otitic hydrocephalus is reviewed and five new cases reported.

(2) The pathological basis of the syndrome is discussed, and it is concluded that infection of the lateral sinus is the most important

ætiological factor, but that obstruction of the sinus is not an essential factor.

(3) It is suggested that mural thrombo-phlebitis of the superior longitudinal sinus, by retrograde extension from the lateral sinus, may, by putting out of action a sufficiently large proportion of the arachnoid villi, be the cause of otitic hydrocephalus.

(4) Cases are recorded from the literature in which hydrocephalic symptoms have been associated with proved thrombosis of the superior longitudinal sinus.

(5) Two cases are reported in which hydrocephalic symptoms were associated with clinical evidence of thrombo-phlebitis not arising from otitis media.

(6) It is, therefore, suggested that otitic hydrocephalus may be the most frequent example of a clinical syndrome which is caused by thrombophlebitis of the superior longitudinal sinus of a degree and extent which are compatible with recovery. Recovery from the hydrocephalic symptoms is the result of organization and canalization of the thrombi.

(7) The occurrence of focal epilepsy, and acute or subacute hemiplegia, with otitis media is discussed, together with the evidence for regarding this complication as due to thrombo-phlebitis involving the superficial cerebral veins.

(8) A case is reported in which the sudden onset of focal cerebral symptoms was the first evidence of thrombo-phlebitis of the superior longitudinal sinus, and of the superficial cerebral veins, in a case of puerperal infection.

(9) A case is reported in which hydrocephalic symptoms were associated with a brachio-facial monoplegia of sudden onset following a peri-tonsillar abscess, and complete recovery ensued. It is suggested that the cause of these symptoms was thrombo-phlebitis of the superior longitudinal sinus with involvement of a tributary vein.

(10) Observations upon the cerebrospinal fluid in proved cases of thrombo-phlebitis of the lateral, or the superior longitudinal sinus are reviewed and are compared with the results of examination of the cerebrospinal fluid in cases with hydrocephalic or focal cerebral symptoms in which the diagnosis of thrombo-phlebitis was not proved, but appeared probable on clinical grounds.

I am indebted to my surgical colleagues at Guy's Hospital and at the Central London Throat, Nose and Ear Hospital for the opportunities of seeing their patients and publishing my observations; to Dr. C. M. H.

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Notices of Recent Publications.

Pathology of the Central Nervous System. By Cyril B. Courville. Mountain View, California: The Pacific Press Publishing Association. 1937. Pp. 344, with 199 illustrations. Price $5.75.

So many small textbooks on the pathology of the nervous system have appeared within recent years that each newcomer must face criticism, not only of its intrinsic value, but also as to whether in manner or matter it fills gaps which the others have left. This question is easily answered for the present volume, which is concerned much more with the larger questions of ætiology and pathogenesis than with the minutiæ of histological detail which are given in other books. The best and fullest chapters are those dealing with purulent infections and with traumatic lesions of the brain and spinal cord. These conditions are so common that the cursory manner in which they are usually considered in textbooks of pathology does scant justice to their importance. The problems of cerebral hæmorrhage and intracranial pressure also receive full consideration. The mode of action of poisons and toxins and the pathogenesis of virus infections on the other hand are scarcely discussed. Another unusual feature of the book is the emphasis laid on the clinical symptomatology associated with lesions of various kinds and in various situations. There is little fresh in this, and its value in a book of this kind is questionable, especially when problems of clinical diagnosis occupy space which might well have been used for a fuller discussion of pathology.

The diagrammatic drawings representing the author's conceptions of pathogenesis are ingeniously conceived and beautifully executed and help to clarify and complete the text.

Étiologie de la Sclérose en Plaques. Par N. Blackman. Paris: Maurice Lavergne. 1936. Pp. 63. Thèse de Paris. Price not stated.

This small monograph is a survey of the experimental and histological work which has been carried on, up to the time of publication, on the ætiology of disseminated sclerosis, and an account of the author's experiences with the reduced silver method of Steiner. In particular he has looked for Steiner's "silver cells" in eleven cases of disseminated sclerosis, five cases of other organic and toxic diseases of the brain, and one normal case. The staining was controlled by staining at the same time the cortex of two cases of general

paralysis in which spirochætes were found. This study confirmed the results obtained by other authors, viz. the presence of "silver cells" in the lesions of disseminated sclerosis in almost every case studied, and their absence in almost every other disease of the brain. However he found similar cells on the edge of foci of hæmorrhage or infarction in three non-syphilitic cases. By the method of micro-incineration he was able to demonstrate the presence of iron and calcium in the "silver cells" in both forms of disease. He considered that "silver cells" were of reticulo-endothelial origin, but does not advance any opinion either as to why they should sometimes stain with Steiner's method, or as to whether the granules stained in them in plaques of disseminated sclerosis are the debris of spirochætes or some other inclusion.

Forme Cérébrale de la Cholesterinose Généralisée. Par L. van Bogaert, H. J. Scherer, and E. Epstein. Paris: Masson et Cie. 1937. Pp. 183. Price 45 Fr.

This interesting monograph is based on the examination of two familial cases of a syndrome which has not been previously described. The cases presented the unusual combination of mental retardation, ataxia later replaced by spasticity and in one case by amyotrophy and bulbar symptoms, with juvenile cataract, xanthelasma, and lipoid tumours in relation to the bones and tendons of the lower limbs. The pathological examination of the first case showed that most of the nervous symptoms could be ascribed to the accumulation of cholesterin in crystalline form in the spinal cord and brain-stem. The tumours also contained masses of cholesterin crystals and the disease, as a whole, appeared to be due to a faulty metabolism of cholesterin.

The pathogenesis of this interesting disease and its relationship to other lipoid dyscrasias are discussed by Epstein of Vienna to whom, owing to his expert knowledge of such conditions, the analysis of the lipoids was entrusted. The other examinations were made by van Bogaert and Scherer and are described in the careful detail which the unique character of the disease merits.

La Hernie Postérieure du Ménisque Intervertébral. Par P. Glorieux. Paris: Masson et Cie. 1937. Pp. 102. Price 40 Fr.

Herniation of the nucleus pulposus of the intervertebral discs has within the last few years attracted much attention as a possible cause of various nervous symptoms. Andrae found evidences of herniation into the canal in 15 per cent. of vertebral columns which he examined at autopsy, but it is obvious that they produce symptoms in a small proportion of cases only. Most of those who have written on the subject assert that neither by clinical methods nor by X-rays can the condition be diagnosed during life, but the

author of this monograph, who is a Belgian radiologist, claims that by the use of lipiodol in the manner he describes the protrusions can be easily demonstrated. The numerous radiographic films reproduced here certainly support his claims, and demand careful study and confirmation by others.

His discussion on the ætiology of the herniations and the various types that may result, particularly from vertebral trauma, is excellent, but his study of the symptoms which may be associated with them is superficial. He emphasizes only pain in the form of lumbago or sciatica, in fact he asserts that a large proportion of all cases of sciatica are due to compression of the roots by lumbar herniations. Although the monograph is pervaded by rather uncritical enthusiasm it deserves attention.

The Intellectual Functions of the Frontal Lobes. By R. M. BRICKNER. New York: The Macmillan Company. 1936. Pp. 354. Price 15s.

Here is a book which presents matter of great interest to neurologists and psychologists. A man from whom a large part of each frontal lobe was removed was carefully observed and investigated by modern psychological methods during the second year after the operations. The only physical disability present was tremor of his head and hands; he had, however, a few epileptic attacks. The mental changes were quantitative rather than qualitative, and consisted chiefly in a difficulty in synthesizing simple mental processes into more complex ones, in fact the author concludes that the frontal lobes play no special rôle in intellectual function, and their loss leads to no primary change in emotional activity. Earlier work on the functions of the frontal lobes, both experimental and clinical, is reviewed and correlated with the author's own observations.

Les Meningiomes Supra-Sellaires. Par L. GUILLAUMAT. Paris: G. Doin et Cie. 1937. Pp. 205. Price 30 Fr.

This admirable contribution to the symptomatology and pathology of suprasellar meningiomas is based on a study of twenty-two cases observed in Clovis Vincent's Clinic. In the early chapters the anatomy of the suprasellar region of the skull is described in detail, for the visual symptoms must depend largely on the point of origin and the direction of growth of the tumour. The symptoms which characterize these tumours are then carefully analysed and their differential diagnosis from other tumours in this region, especially from those arising from the olfactory groove and from the lesser wing of the sphenoid, is discussed. An important point which the author brings out clearly is the difference in the symptoms caused by tumours attached to the tuberculum and by those of more anterior origin.

Sleep Characteristics. By N. KLEITMAN, F. J. MULLIN, N. R. COOPERMAN, and S. TITELBAUM. Chicago: University Press. London: Cambridge University Press. 1937. Pp. 87. Price 4s. 6d.

This praiseworthy attempt to determine the chief characteristics of sleep and how they may be modified by various conditions was undertaken by four members of the staff of the Department of Physiology of the University of Chicago on thirty-six adult subjects, with an average of 179 nights per subject. Their observations bring out many interesting and important facts, and being statistically analysed they will furnish valuable material for future investigations on sleep and its disorders.

Die Epilepsie. Biologie, Klinik, Therapie. von F. FRISCH. Leipzig: Weidmann and Co. 1937. S. 144. Price RM. 8.

On opening a new book on epilepsy the reader naturally looks for new light on the nature of the disease or for new suggestions for its treatment; this volume does not contribute to either of these problems, but it is readable and in certain respects interesting. It has been written for the general practitioner rather than for the specialist, by one who has been in charge of a large epileptic institution.

The Mentally Ill in America. By A. DEUTSCH. New York: Doubleday, Doran and Co. 1937. Pp. 530. Price $3.

In this comprehensive and readable book we are presented with a history of the care and treatment of the insane in the United States from Colonial times till to-day. The fact that it has been written from a social rather than a medical point of view adds to its interest as the author doesn't find himself committed to, or biased by, any prepossessions. He traces the treatment, or rather the neglect, of the insane from the earliest days of American history and where necessary has considered the gradual evolution of their humane and reasonable care in other countries too. Chapters are devoted to the Mental Hygiene movement, which is at present so active in his own country, and those on insanity and the criminal law, and the conditions of certification in America should interest all who have to deal with the mentally ill.

Beiträge zur Entwicklung der Strukturen und Kreuzungen im Zentralnervensystem. von Professor DÖLLKEN. Leipzig: G Thieme. 1937. S. 68. Price RM. 5.80.

This study on the development of the functional elements of the nervous system is concerned largely with the commissures connecting similar or different parts of the two sides and with the decussations of the central

nervous system. In this subject he adds little to what is already known and scarcely contributes to the problem of the decussations, as those of the optic and trochlear nerves. The earlier chapters are devoted to the structure and relations of the intra- and extra-cellular neurofibrils, the part they play in the synapse and the conditions of conduction through them. The author's own findings would have been more valuable if they had been more critically correlated with the observations and conclusions of other workers.

Primitive Intelligence and Environment. By S. D. PORTEUS. New York: The Macmillan Company. 1937. Pp. 325. Price 15s.

The author's interest in the influence of environment on intelligence was apparently first excited by his experience among children of different races born in Hawaii and educated together or under similar conditions. This was followed by his investigations on the aborigines of Australia, the results of which have been published in his "The Psychology of a Primitive People." These are resumed in the earlier chapters of this book, which is, however, devoted mainly to observations on the mentality of certain primitive tribes in South Africa and its dependence on the conditions under which they live; the study of these two primitive peoples promised to bring evidence as to the relative importance of environment and mental equipment in their intellectual status. Though the material already collected enables the author to classify the races so far investigated according to capacities as revealed by special tests, general conclusions are reserved for a future volume. In addition to his scientific observations the book contains excellent descriptions of his travels and of the social conditions of the various tribes he met.

Developmental Abnormalities of the Eye. By I. MANN. Cambridge: The University Press. 1937. Pp. 444. Price 50s.

Many aspects of ophthalmology are so closely related to neurology that this volume on irregularities in the development of the eye, which is characterized by an intimate knowledge of embryology and much original investigation, must claim the interest of students of the nervous system. Its object is to show how congenital defects and disturbances due to them come about. In the chapter on developmental abnormalities of the skull, for instance, the origin of oxycephaly and allied conditions is discussed, while in those dealing with the fundus not only are the congenital anomalies which everyone who uses an ophthalmoscope occasionally meets described, but also many pathological conditions which develop later in life in the eye or in the nervous system on the basis of embryonic disturbances, as Lindau's disease, Leber's optic atrophy and many other affections of interest to the neurologist.

The book is written clearly and concisely, very well illustrated and excellently reproduced.

Perspectives in Biochemistry. Thirty-one Essays presented to Sir F. Gowland Hopkins. Edited by J. NEEDHAM and D. E. GREEN. Cambridge: The University Press. 1937. Pp. 361. Price 15s.

Few of these essays have a direct bearing on neurology, but almost all of them furnish interesting evidence of the recent advances and trends of biochemistry in the realms of biology and medicine. Two articles, however, are concerned with the normal and disordered activity of the nervous system. Quastel, in his essay "Biochemistry and Mental Disorder," touches on several points of practical importance, particularly on the chemical factors involved in treatment by narcosis and by "Insulin Shock." In an essay on "Biochemical Approaches to the Study of the Function of the Nervous System" E. Holmes deals with the chemical problems involved in central nervous activity and the difficulties in their investigation.

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EDITOR.